WHITLA'S
PHARMACY
MATERIA MEDICA
AND
THERAPEUTICS

FOURTEENTH EDITION

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WITH A CHAPTER ON THE USE OF VITAMINS
IN MEDICINE BY

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PREFACE TO THE FOURTEENTH EDITION

In this revision an attempt has been made to keep pace with the rapid advances in the sulphonamide drugs, the vitamins and with the five addenda to the British Pharmacopœia. A section on Biological Standardization has been included in Chapter II.

Unfortunately, while the book was still going through the press—but after he had completed his part in it—my colleague, Mr. E. R. Withell, died; consequently, it is left to me to sign the preface alone.

J. H. BURN.

OXFORD,
March, 1943.

PREFACE TO THE THIRTEENTH EDITION

THE present revision of Sir William Whitla's book of *Pharmacy, Materia Medica and Therapeutics* has departed from previous revisions chiefly in the arrangement of the section of Therapeutics, which is no longer an account of the action of all pharmacopœial substances taken in alphabetical order, but is an attempt to deal briefly with those aspects of pharmacology which have an application in therapeutics. It was felt that the earlier arrangement had the disadvantage of giving too much prominence to details of information of little medicinal value and thereby obscuring the importance of many remedies, of the use of which the doctor is still too little informed. The progress of medicine

has recently become so rapid that a knowledge of the action of specific remedies in the body is now a vital necessity if the doctor is to be able to put at the patient's service the gains of medical science.

The number of substances used in medicine is now so large that an attempt to describe the action of all within the pages of a small book is no longer possible. This task is in fact performed by the two publications of the Pharmaceutical Society, the *British Pharmaceutical Codex*, and the *Extra Pharmacopœia*, and all those who wish to have at hand a reference book in which nearly everything can be found should consult these. We are ourselves indebted to the Council of the Pharmaceutical Society for permission to quote from these books.

In the section of Therapeutics the first six chapters are devoted to the phenomena of variation, the action of hormones and the action of vitamins. The remaining chapters give a brief account of the action of drugs and of substances used in chemotherapy; they have been written with the aim of presenting the medical student with the facts he ought to know for his examinations in a concise and rational form.

The second section on Pharmacy may have the effect on medical readers of persuading them to leave dispensing to pharmacists, but it should be a help to the doctor in writing prescriptions. Dispensing is an art for which much training is required and it is perhaps not sufficiently known that for the last few years a qualified pharmacist or "chemist" has been required to devote two years to training apart from his apprenticeship. Thus there has recently been a greatly increased standard. It is most important that all doctors should be acquainted with the facts set out in the chapter on sterilization, for in spite of much bacteriological training, medical students learn little of the methods of preparing sterile solutions.

Our thanks are due to the Editors of the *Biochemical Journal*, the *British Medical Journal*, the *Journal of Physiology*, the *Lancet* and the *Quarterly Journal of Pharmacy and Pharmacology* for permission to reproduce figures, and also to the authors concerned.

J. H. BURN.
E. R. WITHELL.

August, 1939.

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SECTION I

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CHAPTER I

BIOLOGICAL VARIATION

EVERYONE is aware that men vary in height; the average height is probably about 5 feet 6 inches, but some persons are less than 5 feet high and some are more than 6 feet high. Similarly everyone is aware that the size of feet and hands varies; some have very small hands, and others very large hands. Similarly it is known that there is a variation in the amount of hair; some have much hair, others very little. In general there is no difficulty in recognizing variation where it can be seen, but when it cannot be seen, it is not so readily recognized. Let us take the systolic blood pressure as an example. Current physiological teaching is that the normal systolic blood pressure of man lies between 120 and 130 mm. mercury. Values higher than this are thought to be abnormal, and to indicate disease. If a doctor makes a routine examination of any person he usually determines the systolic blood pressure, and if he finds that this pressure is 150 mm., the doctor tells the patient that he is suffering from hypertension and must modify his diet and mode of life accordingly. Let us suppose, as must often happen, that a blood pressure of 150 mm. is discovered during a medical examination for life insurance; at the beginning of the examination the subject imagines himself to be in good health having no need to give thought to his physical condition. He leaves the examination believing himself to be a sufferer from an insidious disease known as high blood pressure; from that time forward his outlook may be permanently discoloured by this belief.

The question to be considered is whether it is true that a

systolic blood pressure of 150 mm. indicates disease. Now as long ago as 1923 Alvarez published tables showing the variation in systolic blood pressure of persons in the University of California. He recorded the figures for men and women separately, but for the purpose of this discussion we will confine our attention to those for men. There were 6000 men between the ages of 16 and 40 years and the systolic blood pressure of these varied from 85 mm. of mercury as the lowest value, to 194 mm. as the highest. This was a quite unexpectedly large range of variation. Now since the subjects examined varied from 16 to 40 years in age, there was the possibility that the higher blood pressures were due to the existence of disease among the older men. Alvarez therefore recorded separately the pressures in 1216 students all of 18 years of age, and found that the range of variation was almost the same, namely, from 85 mm. to 184 mm. His findings for men of 18 years and for those between 16 and 40 years are given in Table I.

TABLE I

PRESSURE.	AGE.	
MM.	18 YEARS.	16–40 YEARS.
85–89	3	5
90–94	2	18
95–99	3	38
100–104	14	89
105–109	17	122
110–114	79	447
115–119	116	622
120–124	249	1196
125–129	124	650
130–134	232	1104
135–139	100	464
140–144	122	605
145–149	44	179
150–154	57	218
155–159	20	77
160–164	22	93
165–169	4	29
170–174	5	23
175–179	1	10
180–184	1	7
185–189		2
190–194		1
	1216	6000
Mean	130	128·9
Standard deviation	13·4	13·5

When this table is examined it is observed that the number of persons with very low blood pressures is small; the number steadily rises for blood pressures up to 120 mm., and then after 134 mm. the number steadily falls. Between 120 and 134 mm. is clearly the most fashionable range of blood pressure, hence called by statisticians the "mode." To be in this range is to be "*à la mode*." In Fig. 1 a graph has been drawn showing the number of persons (expressed as ordinates)

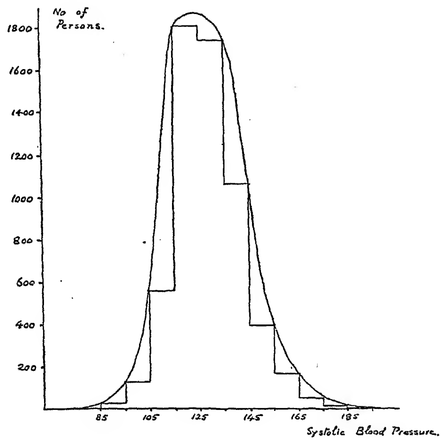

FIG. 1.—The curve shows the relative frequency with which systolic blood pressures within certain ranges are met. Thus out of a total of 6000 persons there were about 600 in whom the systolic pressure lay between 105 and 115 mm.

corresponding to each range of blood pressure; in Table I the number of persons for each range of 5 mm. is given, but in Fig. 1 the number of each range of 10 mm. is given. The diagram in Fig. 1 is known as a frequency curve because it shows the frequency with which persons having a blood pressure within a given range are met. Persons having a blood pressure from 95 to 105 mm. are met much less frequently than persons having a blood pressure from 125 to 135 mm.

The diagram is fairly reliable because it was prepared from observations on no less than 6000 persons. In order, however, to discover the true frequency curve for blood pressure it would be necessary to make determinations on a much larger number of people. If these observations were available a diagram could then be built up showing the frequency with which much narrower ranges of blood pressure are met. The diagram obtained would then approximate to the smooth curve drawn through the points in Fig. 1. The smooth curve shows that it is impossible to give a single figure for the normal systolic blood pressure. There is an average systolic blood pressure which Alvarez found to be 129 mm., but blood pressures below this and above this are still normal, that is to say, they are not pathological. Since the curve in Fig. 1 is continuous it is impossible to say at any point between 85 mm. and 195 mm. that the blood pressure is abnormal, and hence the correct statement to make is that normal systolic blood pressure varies from 85 mm. to 195 mm., the mean or average value being 129 mm.

Variation in Response to Drugs.—The chief value of these figures relating to blood pressure is that, obtained as they have been on a large number of persons, they establish the fact of continuous variation for a biological property which is not visible to the eye. As was said earlier, variation is recognized in visible properties such as height and amount of hair, but it has not hitherto been recognized in invisible properties. But all physiological properties are found to vary in this way on examination and the variation extends also into pharmacology. Thus the response of different persons to a given amount of drug varies in exactly the same way as the height of the blood pressure. Hanzlik, for example, has investigated the variation in the dose of sodium salicylate which produces toxic symptoms in different patients. Sodium salicylate is used in the treatment of acute rheumatic fever when the patient suffers from a high temperature and intense pain in one or more joints. Large doses, of 20 grains or 1·3 gm., given repeatedly are usually required up to a maximum of 180 grains or 12 gm. a day. Now sodium salicylate when used in this way often produces toxic symptoms, which are vomiting, headache and buzzing in the ears. Hanzlik found that among 400 patients some had toxic symptoms after as little as 40 grains and others had none until they had taken

as much as 470 grains. The frequency of the occurrence of toxic symptoms was greatest, however, when doses from 150 to 200 grains had been given. But it is noteworthy that the variation in patients was so great that some were unaffected by ten times the total dose which produced symptoms in others.

A further example of this kind is given by the observations of Paxson (1932) on the amount of sodium amytal required to produce narcosis in women in labour. Sodium amytal (or sodium isoamylethyl barbiturate) was injected intravenously at a slow rate until the required degree of narcosis was obtained, and the amount injected was calculated per kilogramme of the body weight of each patient. In one patient as little as 5 mg. per kg. was sufficient; one patient, however, required as much as 19 mg. per kg., which is almost four times as much; other patients required amounts in between these two extremes, most requiring from 10 to 12 mg. per kg. These results of Paxson show that a mere calculation of dose according to the body weight of the patient does not appreciably diminish the variation in the sensitiveness of different patients. It has long been known, for example, that the response of patients to the action of digitalis, a drug which is used in heart disease, varies considerably. Some clinicians have believed that if they weighed the patient and calculated the dose according to the body weight then the response obtained was uniform. There is no reason to suppose that this is true. It is probably better to administer potent remedies like digitalis according to body weight, but this does not greatly affect the variation in the patients' response.

The Use of Basal Anæsthetics.—Recognition of the extent of the variation in the response of patients to drugs is most important, for ignorance of it is on the one hand dangerous to patients, and on the other hand results in the discarding of useful drugs. This is well exemplified by results with anæsthetics such as nembutal (sodium ethyl methyl butyl barbiturate) and pernocton (sodium butyl-β-bromallyl barbiturate). Anæsthetics may be divided into the two classes, the volatile anæsthetics like chloroform and ether, and the anæsthetics which act in solution and which must be injected, like the two derivatives of barbituric acid mentioned. Soluble anæsthetics have the important advantages that they are much pleasanter for the patient, who goes to sleep while in bed in

the ward before he is taken to the operating theatre, and that they produce much less shock. On the other hand, once a dose of a soluble anæsthetic has been injected, the effect of that dose cannot be undone; if the dose is too large the patient will probably die. Now since there is a very wide range of variation in sensitiveness to derivatives of barbituric acid, as shown by Paxson's results with sodium amytal, there is an obvious danger in the use of nembutal and pernocton and similar substances by a doctor who is unaware of the variation. He may find that a given dose produces a certain desired effect in some patients who happen to be of about average sensitiveness and then give the same dose to a patient who is much more sensitive. The patient then dies. Disturbed by this disaster, the doctor then refuses to use the anæsthetic again, and returns to the volatile anæsthetics, chloroform and ether. It is surely clear that when a soluble anæsthetic is used it must be given only as a basal anæsthetic, that is, to say, in so small a dose as to provide, not complete anæsthesia, but a certain basal anæsthesia, on top of which a small amount of volatile anæsthetic will produce full surgical anæsthesia. Having regard to the wide variation in the sensitiveness of patients, the dose of soluble anæsthetic, if given in one injection at a rapid rate, must be very small. The most suitable procedure is to give the soluble anæsthetic in a series of two or more doses, or best of all as a slow intravenous injection so that there is sufficient time to see the full effect of a given amount of anæsthetic before more is injected.

The Standard Deviation.—Having illustrated the fact of biological variation and having pointed out some of its practical consequences, we may now return to the results of Alvarez for systolic blood pressure. The method of finding the average or mean blood pressure is well known. All the figures for blood pressure are added together and the sum is divided by the number of persons examined. Alvarez got 129 mm. as the average blood pressure of men. We can now find how much each of the 6000 blood pressures recorded differs or deviates from this average. We can then find the average difference or deviation by adding up all these differences or deviations and dividing by the number of deviations. Statisticians, however, are not content to determine the average deviation in this way, but prefer to determine instead what they call the standard deviation, which means very much the

same thing. They calculate the deviation of each blood pressure from the mean and then square it. They add together all the squares obtained, and divide the sum by the number of deviations. They then find the square root of the result. This is the standard deviation. The standard deviation of Alvarez's figures for men was 13·5.

Now it is being found that the variation in all biological properties follows a frequency curve like that shown in Fig. 2. Thus the smooth curve in Fig. 1 is one particular example of the curve in Fig. 2. If B corresponds to the mean value on the abscissa, then DB and BC are each made equal to the standard deviation. If perpendiculars DF and CE are drawn, then the area of AFDCE is found to be approximately twice the sum of the areas FGD and ECH. Now in the observa-

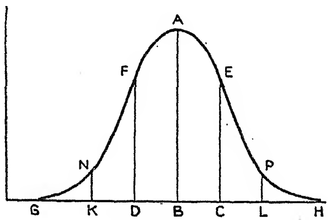

FIG. 2

FIG. 2.—Theoretical frequency curve.

tions on systolic blood pressure the point B corresponds to the mean 129 mm. The point D is obtained by subtracting the standard deviation 13·5 from the mean; hence the point D corresponds to 115·5 mm. Similarly, the point C is obtained by adding the standard deviation to the mean, which gives 142·5 mm. Now the fact that the area AFDCE is twice the sum of the areas FGD and ECH means that if we examine the blood pressure of any healthy man the value found is twice as likely to lie between 115·5 mm. and 142·5 mm. as to be less than 115·5 mm. or greater than 142·5 mm. Or if we examine three healthy men, the blood pressure of two of them is likely to be between 115·5 mm. and 142·5 mm., while the blood pressure of the third will be either less than 115·5 mm. or greater than 142·5 mm. Or if we examine six healthy men, the blood pressure of four of them is likely to

lie between 115·5 and 142·5 mm., the blood pressure of the fifth is likely to be less than 115·5 mm. and the blood pressure of the sixth is likely to be more than 142·5 mm. Thus according to the statistical theory one-sixth of all healthy men are likely to have a blood pressure greater than 142·5 mm. We can compare this conclusion with the observations made by Alvarez. He found actually that 22 per cent. of men had a blood pressure greater than 140 mm., which is not bad agreement between theory and fact.

Returning to Fig. 2, KB and BL are each made equal to twice the standard deviation. If perpendiculars KN and LP are drawn, then the area ANKLP is found to be approximately 21 times the sum of the areas NGK and PLH. If we subtract twice the standard deviation (which is 27) from the mean blood pressure, we find that K corresponds to 102 mm.; similarly L corresponds to (129 + 27 =) 156 mm. Then if we examine the blood pressure of 22 healthy men, we will be likely to find that the blood pressure of 21 of them lies between 102 mm. and 156 mm., while the blood pressure of the 22nd man is either less than 102 mm. or greater than 156 mm. Similarly if we examine the blood pressure of 44 men, the blood pressure of 42 will lie between 102 and 156 mm., while one will have a pressure less than 102 mm. and one will have a pressure greater than 156 mm. Thus according to the statistical theory one man in 44 will have a blood pressure greater than 156 mm. Alvarez actually found that a blood pressure greater than 160 mm. occurred in one man in 36.

These examples of the use of the standard deviation indicate how the probability of variations from the mean occurring by chance may be calculated.

Clearly the ordinary teaching that a normal blood pressure should be 125 mm. or 130 mm. is misleading. How many unfortunate people are going about today under the impression that they are suffering from high blood pressure, when in fact their pressure merely shows an unusual deviation from the mean?

The Significance of a Difference.—In making clinical observations it often happens that a result is obtained which may or may not be significant. For example, in examining the action of a drug, the changes occurring in patients receiving the drug are greater than those occurring spontaneously in

patients not receiving it. What steps can then be taken to discover whether the changes in the patients taking the drug are also spontaneous or are due to the drug?

The results which are now discussed were obtained by students in a class with an apparatus known as a dotting machine. When this machine is in motion a series of small circles come into the observer's view and pass out again at a steadily increasing rate. The observer tries to make a pencil mark inside each small circle as it passes. There are in all 350 circles, and when all have passed the observer counts the number in which he has successfully placed a mark. Each student made three attempts at the beginning of his test; he then drank a liquid, and after half an hour made three further attempts. The liquid was either a ginger-flavoured syrup containing benzedrine, or the syrup without the benzedrine, and the student did not know which of the two he was taking. Five students took the syrup with benzedrine and seven students took the syrup alone. The results are given in Table II. For each student the mean figure for the number of circles hit was calculated both before and after taking the syrup, and the change in the mean figure is given in the last column. The mean change in the mean was 35·2 for students taking the benzedrine while it was 17·3 for those who had syrup only.

TABLE II

1ST GROUP: STUDENTS WHO TOOK SYRUP + 10 MG. BENZEDRINE

	ATTEMPTS BEFORE.				ATTEMPTS AFTER.				CHANGE IN MEAN.
	1ST.	2ND.	3RD.	MEAN.	1ST.	2ND.	3RD.	MEAN.	
A	269	301	—	285	308	313	305	309	+ 24
B	140	201	208	183	219	220	247	229	+ 46
C	177	189	200	189	215	249	244	236	+ 47
D	200	212	228	213	232	238	251	240	+ 27
E	226	270	265	254	289	271	299	286	+ 32

Mean change in mean + 35·2

TABLE II (*Continued*)

2ND GROUP: STUDENTS WHO TOOK SYRUP ONLY

	ATTEMPTS BEFORE.				ATTEMPTS AFTER.				CHANGE IN MEAN.
	1ST.	2ND.	3RD.	MEAN.	1ST.	2ND.	3RD.	MEAN.	
F	270	258	—	264	238	205	194	212	− 52
G	126	202	205	178	196	210	221	209	+ 31
H	159	221	208	196	230	244	266	247	+ 51
J	210	214	247	224	171	271	293	245	+ 21
K	225	236	245	235	194	232	227	218	− 17
L	160	228	229	206	254	260	268	261	+ 55
M	179	231	247	219	226	278	250	251	+ 32

Mean change in mean + 17·3

Among the students who had syrup only there were two in whom the mean was less after taking the syrup. The mean change in the mean has been calculated by finding the algebraic sum of the figures for the change in the mean, and dividing this by the number of students.

The question now arises whether the difference between 35·2 and 17·3 is significant. Does the difference prove that benzedrine improves the performance? To solve this the standard deviation of the individual figures which make up each mean must first be calculated. For the 1st group of students this is shown in Table III.

TABLE III

CALCULATION OF STANDARD DEVIATION IN 1ST GROUP

Mean change in mean = 35·2

	DEVIATION.	SQUARE OF DEVIATION.
A	(35·2 − 24 =) 11·2	125·4
B	(46 − 35·2 =) 10·8	116·6
C	(47 − 35·2 =) 11·8	139·2
D	(35·2 − 27 =) 8·2	67·2
E	(35·2 − 32 =) 3·2	10·2
		458·6

In Table III the sum of the squares of the deviations is 458·6. If the number of students was large we would now divide this figure by the number of students; since there were only five students statisticians recommend that we divide by the number of students less one, that is by 4. The result is 114·6, and the square root of this which is 10·71 is the standard deviation of the individual figures for the different students. The standard deviation is an estimate of the spread of the individual figures around the mean. From it the standard error of the mean can be calculated which will obviously depend upon the number of figures from which the mean is derived; the error will be smaller if the number of figures is large. The standard error is not, however, inversely proportional to the number of figures, but to the square root of the number of figures. The mean of observations on sixteen persons is only twice as accurate as the mean of observations on four. Hence the standard error is $\frac{1}{\sqrt{5}} \times 10{\cdot}71$, which is 4·8. The results in the 2nd Group are now taken and treated in the same way; the standard error is found to be 14·6.

To determine the significance of the difference between the two means 35·2 and 17·3, the difference, which is 17·9, is divided by the square root of the sum of the squares of the standard errors. The sum of the squares of the standard errors is

$$\begin{aligned} 4{\cdot}8^2 + 14{\cdot}6^2 &= 23{\cdot}04 + 213{\cdot}2 \\ &= 236{\cdot}24. \end{aligned}$$

The square root of this number is 15·36. The difference between the two means, 17·9, is now divided by 15·36, and the answer is 1·17. When this answer is less than 2·0, as here, then the difference between the means is not significant, and the results do not prove that benzedrine made any difference to the students. To determine this point more students must be tested. (See Burn, 1937.)

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CHAPTER II

BIOLOGICAL STANDARDIZATION. INSULIN

Biological Standardization.—The principles of biological standardization are rarely understood by medical men, and yet they are very simple. Most people know that the biological activity of hormones, serums and vitamins is measured in units; but they imagine that the unit is the amount of a hormone, etc., which produces a certain effect. This is not so, for a unit when measured in this way is always found to be an inconstant quantity. For example, the least amount of œstrogenic hormone which produces œstrus in one ovariectomized rat may be twenty times as great as the least amount necessary to produce the same effect in another. The foundation of biological standardization is that biological methods must be used for comparative purposes only. It is possible to compare with reasonable accuracy the *relative* strength of two preparations and to say that one is 1·75 times as strong as the other. Moreover, when this comparison is made by different workers in different laboratories in different parts of the world the different results are found to be similar, even though the methods used are not the same in all details.

Biological standardization, therefore, depends on a collection of standard preparations which are called international standards. Should a worker in any part of the world wish to determine the potency of an unknown extract of the posterior lobe of the pituitary, he first obtains a sample of the standard preparation and compares the unknown sample with it. Before the war most of the international standards for hormones and vitamins were held at the National Institute for Medical Research, Hampstead, London, while the standards for serums were held in Copenhagen. The unit of activity was defined by international agreement as being the amount of activity in a given weight of the standard preparation. This weight is purely arbitrary; thus the unit of pituitary (posterior lobe) extract is the amount of activity present in 0·5 mg. of the standard preparation. The unit of insulin is the amount of activity in $\frac{1}{22}$ mg. of the standard preparation, which is crystalline insulin. The number of units in any sample of insulin is then determined by comparing the sample with the

standard preparation and finding out the relative strength of the two. Thus, if 1 c.c. of the sample being tested is found to be equivalent in activity to 1 c.c. of a solution of the standard preparation containing 2 mg., then since this solution of the standard preparation contains by definition 44 units per c.c., it follows that 1 c.c. of the unknown sample contains 44 units.

Thus it is important to understand that the unit of activity is not the amount of material which produces a certain biological effect, but is the activity present in an arbitrarily fixed weight of the standard preparation.

Standardization of Insulin.—Methods of standardization usually fall into one of two classes. The first class contains methods in which the effect of a substance administered to an animal can be measured. Thus, if an injection of insulin is made into a rabbit, a fall of blood sugar follows, and the extent and duration of this fall can be determined by taking samples of blood at regular intervals and estimating the sugar present. The effect of the injection of insulin is proportional to the area of the hypoglycæmia obtained by plotting the height of the blood sugar against the time. Thus this method enables a *quantitative* expression of the effect of the insulin in this rabbit to be obtained. The second class of method is that in which the injected substance produces an effect which cannot be measured. If insulin is injected into a mouse, the mouse will, if the dose be large enough, have convulsions. The convulsions, however, cannot be measured; all that can be said is that the dose of insulin has either produced convulsions, or has failed to do so. This is a method in which the response is *qualitative*.

The Rabbit Method.—To compare a sample of insulin with the standard preparation by the rabbit method, each solution is tested on a group of rabbits. It is necessary to use a group of, say, 10 rabbits for the standard preparation, and 10 rabbits for the unknown sample, since it is necessary to determine the average effect produced both by the standard preparation and by the sample. The test on the two is carried out simultaneously. On the next day or the day after a further test is done on the same rabbits, in which the group which previously received the standard preparation is given the sample, and the group which received the sample is given the standard preparation. The dose of the standard preparation

given to each rabbit on each day is the same, usually one unit, though some workers give a rather higher dose. The dose of the sample, which is also used for all the rabbits to which the sample is given, is a dose expected to contain one unit. In each rabbit, which has been kept without food since the previous evening, the blood sugar is determined before the injection of insulin, and at hourly intervals for five hours after. The figures for one rabbit may be as follows. Initial blood sugar, 0·116 per cent., hourly values after injection 0·085, 0·061, 0·052, 0·073, 0·098. The average of the figures after the injection is 0·074 per cent., and the average degree of hypoglycæmia is therefore the difference between this and the initial blood sugar, namely, 0·042 per cent. For reasons which need not be gone into here this figure is expressed as a percentage of the initial blood sugar and thus we arrive at the result 36·2 as the percentage blood sugar reduction in that rabbit.

The average of all the figures so obtained for the different rabbits injected with the standard preparation is calculated, and similarly the average for the rabbits injected with the sample. If the two averages are identical then it is known that the dose of the sample injected actually contained one unit. If the two averages are not identical, previous experience has given information what particular difference in the potency of the sample from one unit would have produced the difference in the results. The whole experiment is then repeated adjusting the dose of the sample so as to obtain results with it as nearly equal to those obtained with the standard preparation as possible.

The Mouse Method.—When insulin is to be tested on mice, use is made of the fact that if the mice are kept at a temperature of 37° C. insulin produces convulsions in the mice, and the percentage of mice in which convulsions occur bears a relation to the dose of insulin which is shown in Fig. 3. Inspection of the figure shows that the curve has approximately an S-shape, and that the percentage rises most rapidly in relation to the dose in the neighbourhood of 50 per cent.

The method of carrying out the test is very simple. A group of mice is injected with a chosen dose of the standard preparation, and a similar group is injected with a dose of the sample. The mice are at once put in an apparatus where the air temperature is carefully regulated to be 37°, and the percentage of mice which have convulsions is determined in each group during the next hour. Further experiments are then carried

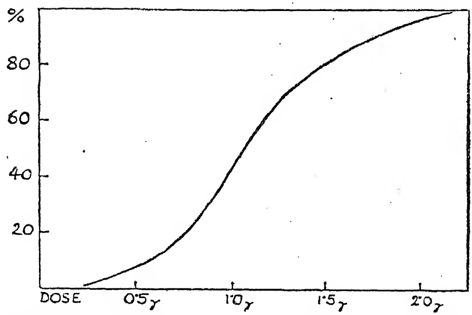


FIG. 3.—Relation between dose of insulin and percentage of mice convulsing.

out until a dose of the sample is found which produces convulsions in the same percentage of mice as the chosen dose of the standard preparation, this percentage being not far removed from 50 per cent.

Methods Giving a Quantitative Response.—The determination of the potency of a sample of insulin by the rabbit method is an example of a method in which the response measured is quantitative. It is a general rule about all such methods that the effect produced is directly proportional to the logarithm of the dose of the substance injected, though not to the dose itself. This is true, for example, of insulin where it is found that if the logarithm of the dose of the sample is plotted graphically against the effect, then over a certain range of dosage a straight line is obtained. This linear relation of the logarithm of the dose to the effect is true for many other hormones such as prolactin, the thyrotropic hormones, for vitamins such as vitamin A, B_1 and C, and also for the effect of chemotherapeutic substances like that of neoarsphenamine on trypanosomes.

The relation can be applied in the following way. To compare the effect of a sample with a standard preparation, two doses of the standard preparation are chosen and each dose is given to a group of animals. The average effect of each dose is then observed. At the same time a dose of the sample is chosen likely to give an effect intermediate between the effects of the two doses of the standard preparation. This dose is

also injected into each of a group of animals. The logarithms of the doses of the standard preparation are then plotted as abscissæ and their effects as ordinates, as in Fig. 4 and the

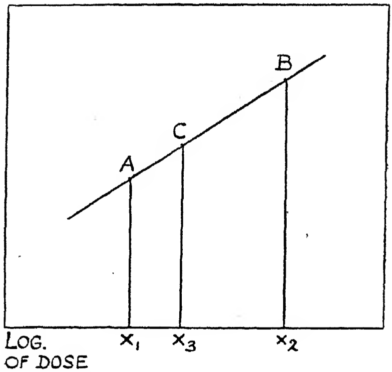


FIG. 4.—A and B represent the average effects of two doses of the standard preparation the logarithms of which are x_1 and x_2. C is the effect produced by a dose of the unknown preparation which is equivalent to a dose of the standard the logarithm of which is x_3.

points joined by a straight line. The average effect of the sample is marked on this line, and the abscissa corresponding to this point is observed. This abscissa is the logarithm of the dose of the standard preparation which would have had the same effect as the dose of the sample. Thus the sample can be equated to the standard preparation.

Methods Giving a Qualitative Response.—When the effect of the substance cannot be measured, the effect of the dose must be judged by the percentage of animals in which an effect occurs. For example, whenever the toxicity of an agent is investigated, either by giving it by mouth or by injection, it is usually necessary to determine not the minimum lethal dose, since this is a very variable quantity, but the dose which produces an effect in 50 per cent. of animals. If the effect is death this dose is commonly referred to as LD 50. LD 80 would be the dose which kills 80 per cent. of animals. The general relationship is indicated by Fig. 5.

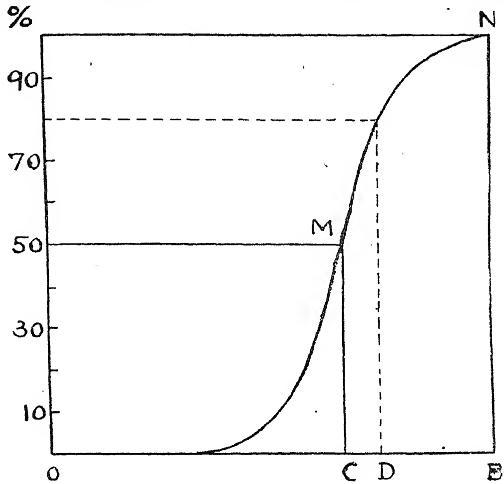


FIG. 5.—The curve AMN shows the relation between dose (abscissæ) and percentage mortality (ordinates). A range of doses, represented by OA, has no effect on any animal ; OC kills 50 per cent., OD kills 80 per cent.

Experimental Diabetes.—Minkowski showed that excision of the pancreas causes a rapidly fatal diabetes ; after removal in the dog there is a rise in blood sugar or hyperglycæmia, and a glycosuria. As the sugar passes down the tubules of the kidney in amounts too large to be reabsorbed, it prevents the reabsorption of much water also, and hence causes polyuria in addition to glycosuria. The polyuria is followed by great thirst. There is a loss of glycogen from the liver, and ketosis occurs, namely, there is a formation of acetoacetic acid and β-hydroxybutyric acid in the blood ; this formation is followed by ketonuria. There is also a fall in the respiratory quotient to a value in the neighbourhood of 0·7 which indicates that all the oxygen used is not reappearing in the expired air as carbon dioxide.

If insulin is injected into a depancreatized animal these changes are inhibited. The hyperglycæmia is reduced and

in consequence the glycosuria stops. The respiratory quotient rises, and the ketosis is arrested. Glycogen reappears in the liver.

The Treatment of Human Diabetes.—For the treatment of diabetes in general practice, Himsworth (1936) gives the following rules. First, eliminate and keep absent all trace of ketonuria; second, remove or reduce glycosuria to the smallest proportions. It is important to realize that ketonuria is a much more dangerous symptom than glycosuria, for a patient who has ketonuria may pass into coma with very little warning. When a patient is discovered to have diabetes, the doctor must decide whether he is to start with insulin at once or not. A good rule is to be guided by the ferric chloride test for ketonuria. If this is positive, insulin must be given at once; if this is negative, insulin is not given at once and the doctor must investigate the patient's reaction to a strict diet.

Diabetic Diets.—It is important to impress on the patient the necessity for strict control of diet and for learning to judge the calorie values of the food he eats. He must weigh his diet every day for the first week, every other day for the next fortnight, twice a week for the next month and thereafter once a week, on Sundays. This stringent control is necessary because it is impossible to judge at first sight which cases will be mild and which severe; it is better to institute a strict regime at first when the patient is amenable, and then to slacken the restrictions later.

As a rule a patient's minimum requirement of food in calories can be judged approximately from his general appearance. An active man can usually manage with 2300 calories per day; a sedentary man with 2000 calories per day; most women with 1750, and some individuals with 1500 calories per day. The diet of 2000 calories, for example, contains 200 gm. carbohydrate, 100 gm. protein and 100 gm. fat.

The doctor should obtain four diabetic diet charts, one for each of these calorie totals; they are constructed so that a patient will have glycosuria before ketonuria. If the patient looks as though his final requirement will be 2000 calories, he is started with 1500 calories and required to collect specimens of urine, half an hour before and half an hour after each of the meals, breakfast, dinner and supper. After eating the diet for 48 hours, the samples of urine are tested for acetone bodies by Rothera's test, and if they are present in all samples,

insulin treatment is begun. If acetone bodies are not present in all samples, the patient continues with the diet for 5 days more without insulin, when his specimens of urine for one day are examined again. If acetone bodies are present in any one of the specimens, insulin treatment is begun. If acetone bodies are not present at all, the patient is given the next diet higher in the scale, and kept on this for one week. If acetone bodies are still not present, he is then raised to the diet which the doctor has decided is sufficient for his needs, and if acetone bodies are absent after one week, the patient is said to be balanced. But if acetone bodies are present in the urine when the diet is insufficient for the patient, insulin treatment is begun.

Insulin treatment is begun with 5 units before breakfast and again before supper. After four days the urine is examined for sugar and if necessary the dose of insulin is increased to 10 units. The insulin dosage should be just sufficient to keep four of the six daily urine specimens sugar-free when the patient is receiving his full complement of calories. The doctor should not attempt to keep the urine entirely sugar-free, for to do so the patient would have to be a semi-invalid, for exercise would bring on hypoglycæmia. It is important that the patient's body weight should be steady at a suitable level. If glycosuria has been restricted, a fall in weight means that the diet is unsatisfactory. If, on the other hand, the weight increases too far, there may be a breakdown in carbohydrate tolerance.

If the patient has an intercurrent illness, the urine must be kept absolutely free from acetone, and the infection must be treated as quickly as possible; often more carbohydrate and more insulin are required.

The Use of Zinc Protamine Insulin.—One of the disadvantages of ordinary insulin is that it acts very rapidly, and that its effect does not last very long, and many efforts have been made to render the action slower and more prolonged. Protamine insulin (sold as Insulin Retard) was introduced by Hagedorn as a combination from which the insulin would be liberated only so fast as the combination broke down in the subcutaneous tissues. As a result of the discovery that crystalline insulin was a zinc salt, made by Scott in Toronto, it was found that when insulin and protamine were mixed in the presence of zinc chloride, a still firmer combination

resulted with a still slower action. Table IV shows the relative rapidity and relative duration of the action of the three forms.

TABLE IV

	TIME TO MAXIMUM EFFECT.	TIME IN WHICH ACTION COMPLETED.
Insulin	2–3 hours	6 hours
Protamine insulin . .	6–10 ,,	12–18 ,,
Zinc protamine insulin .	8–15 ,,	24–30 ,,

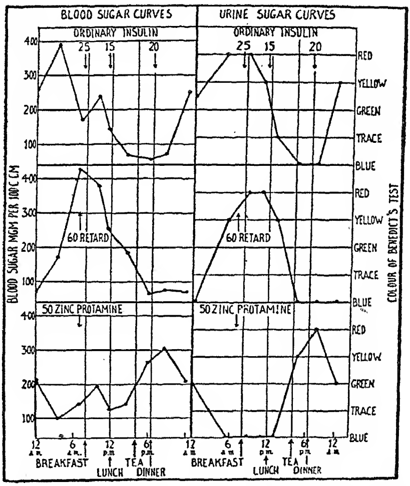


FIG. 6.—Blood sugar and urine sugar curves showing the effects of ordinary insulin, insulin retard (protamine insulin) and zinc protamine insulin, taken from the same patient while on the same diet. (Himsworth, 1937.)

Two advantages of zinc protamine insulin and of protamine insulin are that they make possible a much better control of the disease during the night and reduce the number of injections. Fig. 6 taken from Himsworth (1937) shows the

differences in the blood sugar and urine sugar of a patient treated at different times with these two forms of insulin, and also with ordinary insulin. With 60 units of ordinary insulin, given in three injections, the blood sugar was over 0·2 per cent. during the night, when it reached 0·4 per cent., and also in part of the forenoon. Only in the afternoon was it low, and then appreciably below 0·1 per cent. That is to say, in spite of the three injections the blood sugar was much too high during the night, and because of the three injections much too low in the afternoon. When 60 units of protamine insulin was given as a single injection, the blood sugar was low during the first part of the night, but by breakfast time it had risen to 0·4 per cent.; not till the afternoon did it fall to the neighbourhood of 0·1 per cent. Thus with protamine insulin there was a partial control of the diabetes during the night. With 50 units of zinc protamine insulin given as a single injection the variations in blood sugar during the day were much less. Only during the afternoon and evening, between 4 and 8 o'clock, did the blood sugar rise above 0·2 per cent., and then only to 0·3 per cent. Otherwise it remained between 0·1 and 0·2 per cent. throughout the day and night.

A third advantage of protamine and zinc protamine insulin is that their slowness of action minimizes the risk of hypoglycæmic attacks; the patient's blood sugar level is also less affected by exercise than when ordinary insulin is used.

The disadvantage of the protamine insulin is that when hypoglycæmia occurs during their use, it is severe and prolonged. Moreover, the onset is sudden; the fall in blood sugar is so gentle that warning symptoms do not occur, and the patient finds himself in the middle of an attack without having been able to take sugar.

A further disadvantage arises from the fact that the susceptibility of the body to ordinary insulin is least in the morning and greatest in the middle day. A single dose of protamine insulin in the morning is not able to restrain the rise of blood sugar after breakfast, since the action is too slow; if the dose is increased in an attempt to prevent this rise, then hypoglycæmia occurs in the middle of the night.

Administration of Zinc Protamine Insulin.—Probably the best method of giving zinc protamine insulin is to give it as a single dose before breakfast together with a dose of ordinary insulin; the two can be mixed in the same syringe

immediately before injection. The ordinary insulin acts quickly and prevents the rise of sugar after breakfast, while the zinc protamine insulin keeps the blood sugar low in the afternoon and during the night. If it is found that the period between the effect of the ordinary insulin and that of the zinc protamine insulin is too long, then protamine insulin should be used instead of the zinc protamine insulin.

Treatment of Diabetic Coma.—Two quite different conditions have been confused under the name of diabetic coma. The first is true diabetic coma due to excess of acetoacetic acid and β-hydroxybutyric acid in the blood. This is sometimes referred to as hyperglycæmic coma because it is accompanied by a high blood sugar. The term is unfortunate because it leads some to think that the coma is due to the high blood sugar, whereas in fact it is due to the ketosis. The second condition sometimes called diabetic coma is that of hypoglycæmia in which the subject is unconscious because of the low blood sugar. There is no ketosis.

True diabetic coma due to ketosis is usually accompanied by severe dehydration so that the patient has sunken eyes and hollow cheeks with the smell of acetone in his breath. Treatment must be directed to removing the ketosis and to replacing the fluid. If the patient can swallow fluids given by mouth the treatment is simple, provided large doses of insulin are given. At least 50 units should be given subcutaneously at once, for patients in coma are extremely resistant to insulin. When the patient is in deep coma 50 units of insulin are given together with two pints of 5 per cent. glucose saline solution by slow intravenous infusion. In addition 20 units of insulin are given hourly until the ketosis is checked. As much as 400 units are sometimes necessary. The administration of this insulin must be accompanied by the administration of glucose in the proportion of 2 gm. for each unit insulin.

In the treatment of unconsciousness due to hypoglycæmia, sometimes referred to as hypoglycæmic coma, the remedy is to administer glucose. It may be necessary to give this intravenously. If ever there is doubt whether a patient is suffering from coma due to ketosis or from hypoglycæmia, it is always right to give intravenous dextrose. If the symptoms are due to a low blood sugar they will at once disappear. The treatment of unconsciousness in a diabetic patient must always be undertaken without any delay.

CHAPTER III

THE SUPRARENAL GLANDS

Effects of Adrenalectomy.—If the suprarenal glands are removed from animals, the animals usually die. Death may follow rapidly as in the dog and in the duck, or it may follow more slowly as in the cat, or it may not occur at all as in the adult rat fed on bread and milk. In the duck, adrenalectomy is followed by death at a mean time interval of 8 hours ; in the cat the mean time interval is 8 days. The symptoms of suprarenal deficiency in the cat are loss of appetite, muscular weakness and fall of body temperature.

Now the suprarenal glands consist of two parts, the cortex and the medulla, which secretes adrenaline. Removal of one gland and destruction of the medulla in the other does not cause death in the cat ; the destruction of the medulla is accomplished by cutting off one pole of the gland and destroying the medulla with a dental burr. Evidently the symptoms and death result from the removal of the suprarenal cortex.

Control of Water and Salt.—After adrenalectomy there is a rise in the excretion of sodium chloride, and a retention of potassium. The loss of sodium chloride from the body is of great importance because it is due to this loss that death follows adrenalectomy in the dog. Whether this is true for the duck is not known. Adrenalectomized dogs can be kept alive indefinitely if they are given sufficient sodium chloride and sodium citrate in the diet, and if the potassium in the diet is kept very low. Cortical extract must be given during the period immediately after the operation, but later it can be discontinued. Dogs so maintained are not, however, normal, and if they are given exercise on a treadmill, they at once show signs of cortical deficiency and collapse.

In human subjects disease of the suprarenal cortex is known as Addison's disease, of which the symptoms are pigmentation of the skin, great muscular weakness and low blood pressure. In them also the loss of sodium chloride in the urine is of great importance, for their symptoms can be controlled for long periods by giving 10–15 gm. sodium chloride in the daily diet

Kendall believes that the toxic symptoms which arise from removal of the suprarenals are due not so much to the loss of sodium chloride as to the failure to excrete potassium and the consequent rise in the concentration of potassium in the blood plasma; he considers that the value of giving large amounts of sodium chloride is to cause diuresis and so to wash out the potassium which would otherwise accumulate. Swingle believes that the symptoms of cortical deficiency are due to a reduction of the total volume of the blood plasma, rather than to the excretion of a large amount of sodium chloride, for the symptoms occur when the chloride concentration in the plasma is normal; nevertheless, the symptoms occur only after the loss of much chloride in the urine.

Changes in the excretion of sodium, of chloride and of potassium can be produced in normal dogs by the injection of cortical extract. Table V, taken from a paper by Thorn, Engel and Eisenberg (1938), shows the urinary excretion in three periods of 24 hours each. 10 c.c. of cortical extract injected in the second period reduced the excretion of sodium and of chloride, but increased that of potassium. In the third period the sodium and chloride excretion was greater than in the first period, exceeding that amount by more than the amount retained in the second period. Thorn and his colleagues (1937) have shown that cortical extract causes a similar retention of sodium and chloride, and a similar excretion of potassium in patients with Addison's disease.

TABLE V

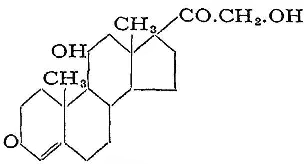
EFFECT OF CORTICAL EXTRACT ON EXCRETION IN THE NORMAL DOG

INJECTION.	URINE VOLUME.	SODIUM.	CHLORIDE.	POTASSIUM.
	c.c.	m. eq.	m. eq.	m. eq.
None	455	51·6	49·8	16·5
10 c.c. cortical extract	545	30·5	34·0	21·3
None	625	86·6	79·2	10·3

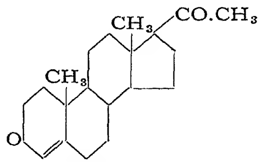
Effect of Sex Hormones on Water and Salt Excretion.—No less than four crystalline substances have been isolated

from the suprarenal cortex, and the chemical structure of one of these, known as corticosterone, is very similar to that of the sex hormones, being particularly close to that of progesterone, which is the hormone of the corpus luteum. The relationship is shown in Table VI. Thorn and his colleagues have therefore investigated how far these closely related substances are able to affect salt excretion in the dog, and have found that œstradiol (5 mg.), œstrone (10 mg.), progesterone (15 mg.) and testosterone propionate (100 mg.) when injected cause a retention of sodium and of chloride which does not

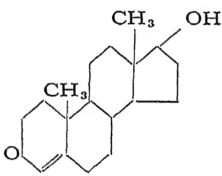
TABLE VI



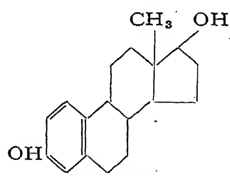
Corticosterone



Progesterone



Testosterone



Œstradiol

occur at once, as when cortical extract is injected, but which reaches its maximum in 2–3 days. The retention is accompanied by diminished urine volume. Now various workers have described the occurrence of generalized œdema in women at certain periods of the menstrual cycle, an œdema which disappears during menstruation. Thorn, Nelson and Thorn (1938) have made observations on women with an accurately controlled diet and water intake and have observed a decrease in the renal excretion of sodium and chloride during the period preceding menstruation; the onset of menstruation was accompanied by an increased excretion. They think it

likely that the retention of sodium and chloride was due to the progesterone formed by the corpus luteum in the premenstrual period exerting an effect like that of the cortical hormone, and that this ceased to function when menstruation began. Thorn states that pseudo-pregnancy and pregnancy itself prolong the life of adrenalectomized animals, and he considers that here also the corpus luteum by forming progesterone is producing a substance which acts as a partial substitute for the cortical hormone.

Carbohydrate Metabolism.—That the suprarenal cortex has some relation to carbohydrate metabolism is suggested by the work of Long and Lukens (1936). They found that when adrenalectomy was carried out at the same time as removal of the pancreas the survival period of cats was prolonged, and the diabetic symptoms, in particular the ketonuria, were much less. The prolongation of life due to adrenalectomy was nothing like so great as that due to simultaneous removal of the pituitary and the pancreas (Houssay 1929), but the diminution of ketonuria was striking. If removal of the cortical hormone by adrenalectomy diminished diabetic symptoms, then injection of cortical extract should aggravate these symptoms. Lukens and Dohan (1938) have now published some evidence that large doses of cortical extract do increase the symptoms of dogs from which pancreas and suprarenal glands have been removed; the evidence, however, is incomplete.

Intestinal Absorption.—Verzar and his co-workers have investigated the effect of removal of the suprarenal glands in the rat upon the absorption of dextrose and of fat from the intestine. When dextrose is given by stomach tube to rats, a dose of 2·0 gm. in 50 per cent. solution causes the death of almost all adrenalectomized rats of about 100 gm. weight. Verzar explains this as due to the failure of the selective absorption of dextrose, so that the dextrose remains in the alimentary canal, withdraws water from the blood of the rat by its osmotic pressure, and causes fatal diarrhœa. Verzar finds that in normal animals dextrose is much more easily absorbed through the wall of the intestine than, for example, xylose, and hence speaks of a selective absorption by the epithelium of the intestine; after adrenalectomy this difference between dextrose and xylose disappears, and much less dextrose is

absorbed than before. By injecting cortical extract the power of selective absorption reappears.

When fat, in the form of olive oil, is given by mouth to an adrenalectomized rat it is not absorbed, and if the animal is killed and the mesentery is examined the lacteals are empty. In a normal rat the lacteals are visibly full of absorbed fat. Verzar thinks that the mucous membrane has lost the power of resynthesizing the fatty acids to neutral fat. By giving cortical extract to an adrenalectomized rat the normal fat absorption occurs again.

During poisoning by phosphorus or carbon tetrachloride in a normal animal, fat is transported from the body stores to the liver. This transport of fat does not occur in an adrenalectomized rat. If, however, cortical extract is injected, the fatty infiltration of the liver takes place as before. There is also said to be some evidence that the formation of ketone bodies does not occur in the adrenalectomized animal.

Verzar believes that the hormone of the suprarenal cortex is responsible for the conversion of lactoflavine to flavine phosphoric acid, which then becomes the yellow respiration ferment. Young adrenalectomized rats can be kept alive without cortical extract if given full yeast extract or liver extract; this is not because of vitamins B_1 or B_4 or B_6, nor because of lactoflavine (which is vitamin B_2), but because of flavine phosphoric acid. Large doses of lactoflavine produce, at most, temporary growth and do not prevent death, while doses so small as 40 γ of flavine phosphoric acid maintain life for a long time, so that the animals reach full size. This view of the function of the suprarenal cortex receives support from the observation that in both normal rats and normal cats, the liver, the kidneys and muscle contain about ten times as much flavine phosphoric acid as free flavine. After adrenalectomy the total amount of flavine diminishes, and the amount of flavine phosphoric acid is not more than the amount of flavine. Full extract of yeast, or flavine phosphoric acid, not only maintain the life of adrenalectomized animals, but influence favourably dextrose absorption and fat absorption.

Poisoning with iodoacetic acid in many respects resembles the effect of adrenalectomy, especially in affecting absorption, and poisoning with iodoacetic acid arrests intermediary metabolism at those points on which the yellow respiration ferment exerts its action. Animals poisoned with iodoacetic

acid can be recovered either with lactoflavine plus cortical extract, or with flavine phosphoric acid without cortical extract.

Thus Verzar believes that the main function of the cortical hormone is to bring about the phosphorylation of lactoflavine; when cortical extract is absent and no phosphorylation takes

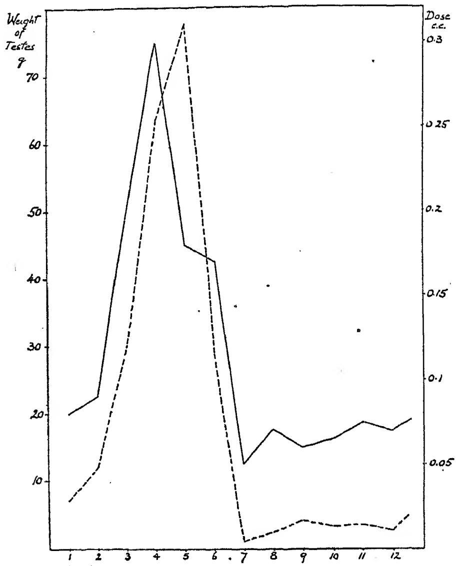


FIG. 7.—Showing the relation between the dose of cortical extract required to keep adrenalectomized drakes for a given time (continuous line, ordinate on right) and the mean weight of the testes (broken line, ordinate on left). The abscissa shows the months of the year. January is 1, etc. (Bülbring, 1937.)

place, the body suffers from a lack of the yellow respiration ferment. This view is not yet, however, everywhere accepted.

The Relation to the Sex Glands.—A relation between the suprarenal glands and the testes is known to exist in their

common embryological origin and in the pathological condition known as virilism. In virilism, which occurs in women, the development of male secondary sexual characters, such as the growth of a moustache, is due to a tumour of the suprarenal cortex, and these characters disappear when the tumour is removed.

Recently Bülbring (1937) has described a relation between the amount of cortical extract required to maintain the life of adrenalectomized drakes, and the size of the testes. From July to December the amount of extract required remains at a uniform low level; in this period also the mean weight of the testes is low, being about 2–4 gm. (See Fig. 7.) From January to April the amount of extract required rises, until about four times as much must be given, and then during May and June again declines. The weight of the testes similarly rises from January to May when the mean weight of the testes is 78 gm.; it then falls again rapidly in June. The parallel between the requirement for extract and the size of the testes may indicate that the testes require the cortical hormone for their normal function in amounts proportional to their size, or that the hormone from the testes increases bodily activity and metabolism in proportion to the amount liberated, and that an increased metabolism requires increased cortical hormone.

The Relation between the Pituitary and the Suprarenal Glands.—Certain metabolic effects appear to be exerted not only by the anterior lobe of the pituitary body, but also by the suprarenal cortex. Thus the diabetes which results from removal of the pancreas is diminished in severity if either hypophysectomy or adrenalectomy is also performed. Now it is known that if the pituitary body is removed the suprarenal glands atrophy to one-half their normal size or less; can it then be that the effects of hypophysectomy on metabolism are a secondary consequence of the effect on the suprarenals? In other words, has the pituitary body no direct effect itself on metabolism? It is impossible to suppose that the effect of the pituitary body is indirect, because the effect of hypophysectomy is so much greater than that of adrenalectomy. The observations of Long and Lukens themselves, who alone have demonstrated the beneficial effect of adrenalectomy on pancreatic diabetes, show that this effect is nothing like so great as the beneficial effect of hypophysectomy at least on

prolongation of life. We must suppose therefore that so far as carbohydrate and fat metabolism are concerned, the anterior lobe and the suprarenal cortex independently produce hormones exerting a similar effect. Knowledge is still much too incomplete for any final conclusion about their relative importance.

Treatment of Addison's Disease.—The treatment of Addison's disease is by means of the addition of sodium chloride to the diet, and also by the injection of cortical extract. So long as possible cortical extract is withheld and sodium chloride used alone in doses of 10 to 15 gm. daily. Usually there comes a point where after months, or it may be after years, sodium chloride is insufficient to ward off a crisis, and cortical extract is then given. The effect of an injection is unfortunately transient, and repeated injections are necessary. Some clinicians believe that the preparations of cortical extract which are available in medical practice are very weak, and that progress in the treatment with cortical extract will not be made until more concentrated extracts are prepared. In the body, however, the extract is rapidly excreted or inactivated, and it is this rapid inactivation rather than the weakness of the extract which makes successful treatment difficult. If some means could be found whereby the hormone could be slowly liberated at the site of injection, progress would then follow.

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CHAPTER IV

THE SEX HORMONES

Œstrogenic Substances.—It was shown by Long and Evans that, when the ovaries are removed from a rat, a cycle of changes which normally takes place in the vagina of the adult rat ceases. The cycle consists of a periodic thickening of the vaginal wall which becomes covered by stratified epithelium; the animal is then in œstrus or heat and will copulate with the male. The thickened vaginal wall is then cast off; the cycle reappears about every four days. Allen and Doisy demonstrated that the changes leading to œstrus could be produced by the injection of ovarian extracts, and that the ovary contained œstrogenic substances, i.e. substances capable of producing œstrus. One of these substances, œstradiol, has been isolated from the ovaries, and other substances having the same property, œstriol and œstrone, have been obtained from the urine. Apparently œstradiol is converted by the body into the other two by oxidation, possibly in the course of acting. There is a further stage before actual excretion in the urine, namely that of conversion into water-soluble substances by linkage with sulphuric acid or glycuronic acid; this is the normal way of getting rid of unwanted hydroxy compounds.

Œstrogenic substances not only produce vaginal changes in the rat, but they also cause the uterus to enlarge and become filled with fluid; thus the uterus and vagina undergo those changes which facilitate the fertilization of an ovum. If œstrogenic substances are injected into immature rabbits the uterus increases in diameter three or four times with enlargement of the endometrium (Fig. 8); the endometrium, however, remains compact; there are a few glands evenly distributed throughout the stroma and the epithelial lining is almost unbroken by glands.

In the human subject there is a menstrual cycle. The first day of the cycle is the day when the menstrual flow of blood and endometrial tissue begins; it continues usually for four days. From the 5th to the 14th day of the cycle is a period in which as a consequence of œstrogenic activity there is a

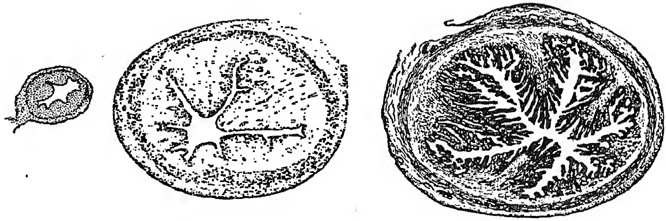


FIG. 8.—The section on the left shows the cross-section of the uterus of an immature rabbit. In the middle is the cross-section after treatment with œstrone ; on the right is the cross-section after treatment with œstrone and progesterone. (McPhail, 1934.)

development of a new endometrium ; a connective tissue stroma is built up in which are found straight tubular non-secreting glands with columnar epithelium. During the same period one of the primordial follicles in the ovary develops into a Graafian follicle, increasing in size until it protrudes from the surface of the ovary.

Progestin Activity.—About the 14th or 15th day of the normal cycle the Graafian follicle bursts and an ovum passes down the Fallopian tube into the uterus. The empty follicle is then filled up by the cells of the membrana granulosa growing centripetally, and so is transformed into a corpus luteum. The corpus luteum produces a hormone which has been isolated as progesterone. This affects the endometrium of the uterus so as to prepare it to receive and nourish a fertilized ovum. In the rabbit the development of the stroma is shown in Fig. 19 ; the changes are known as progestational proliferation, i.e. proliferation in preparation for gestation. In the human subject the glands in the stroma become spiral, and the epithelial cells lining them are filled with secretion so that the nuclei are flattened. The stroma cells are transformed from connective tissue fibroblasts to polyhedral cells with a large central nucleus. These changes go on under the influence of the corpus luteum hormone until the 27th or 28th day of the cycle, when the corpus luteum shrinks and disappears. A new cycle then begins with the breakdown of the endometrium and the menstrual flow.

Observations on Ovariectomized Monkeys.—Knowledge of the part played by œstrogenic substances on the one hand and by the luteal hormone on the other has come in the main from observations on ovariectomized monkeys, made by Zuckerman. Rhesus monkeys (Macaca mulatta) have a menstrual cycle like human beings, which is arrested by removal of the ovaries. The injection of the luteal hormone only for 14 days into an ovariectomized animal does not produce vaginal bleeding, either during the injections or after they have stopped, a fact which agrees with the view that the luteal hormone has little or no effect on an endometrium which has not previously been acted on by an œstrogenic substance.

If an œstrogenic substance such as œstrone is injected, then provided the amount injected is above a certain daily minimum (which varies in different animals from 0·0025 mg. to 0·015 mg.) the cessation of the injections is followed after an interval by uterine bleeding. Thus if œstrone is injected for 14 days, and the injections are then stopped, uterine bleeding occurs, on the average, on the 22nd day. Zuckerman was, however, able to produce cyclical bleeding every 28th day by injecting increasing doses of œstrone during 14 days up to 0·3 mg., and thereafter injecting much smaller daily doses, each about 2–5 per cent. of the previous maximum daily dose. In the human menstrual cycle ovulation usually occurs about the 14th day, and thereafter a corpus luteum is formed; sometimes, however, ovulation does not occur at all, and a corpus luteum is not formed; nevertheless there is menstrual bleeding about the 28th day. This form of menstruation appears to correspond with bleeding induced by the injection of œstrone in the manner described.

When œstrone is injected for 14 days with doses reaching a maximum of 0·3 mg. daily, and progesterone is then injected in doses of 2·0 mg. daily, the uterine bleeding which ordinarily follows one week after the cessation of the œstrone injections is inhibited and remains absent until the progesterone injections are stopped. When the progesterone injections are stopped bleeding occurs in one or two days, and cannot be prevented by the resumption of the injection of large doses of œstrone.

The simplest explanation of the hormone activity during the normal menstrual cycle would therefore seem to be that increasing amounts of an œstrogenic substance act in the

first fortnight after the termination of the last menstruation; the œstrogenic substance is then no longer formed and the luteal hormone acts instead until a day or two before the next menstrual period. Zuckerman, however, points out that this explanation does not account for the 28-day period observed when ovulation does not occur and when no luteal hormone is produced; he believes that an œstrogenic substance acts in high concentration until ovulation takes place, and must then continue to act in much lower concentration together with the luteal hormone.

Urinary Excretion.—Much work has been done on the excretion of œstrogenic substances in the urine from which both œstrone and œstriol have been isolated. Œstrogenic substances occur in similar amounts in the urine of men as well as of non-pregnant women; in pregnant women they occur in large amounts, for example up to 20 mg. œstriol daily. Many other statements are made but are unreliable since the methods of extracting œstrogenic substances from the urine are unsatisfactory. The luteal hormone is not found in the urine, but a transformation product of progesterone, namely pregnanediol, has been found in the urine during the second half of the menstrual cycle, coincidently with the presence of the corpus luteum. Further, when progesterone is injected into human patients, pregnanediol glycuronide can be recovered from the urine in amounts corresponding to 12–46 per cent. of the injected progesterone.

Treatment of Amenorrhœa.—Since œstrogenic substances play so large a part in producing the menstrual cycle they would be thought to be of value in the treatment of amenorrhœa, which is the condition in which the menstrual flow stops. Amenorrhœa is, however, often one symptom of a general condition such as tuberculosis, and it is then wrong to seek to restore the menstrual flow. Often also amenorrhœa occurs because of a lowered metabolism, and is cured by the administration of thyroid. In a small proportion of patients, however, amenorrhœa, having arisen because of a temporary failure of the production of œstrogenic hormone, continues because during this failure the endometrium has diminished in sensitiveness to the action of the hormone, and does not proliferate. The sensitiveness can again be raised by the administration of œstradiol benzoate, but large doses are

necessary, of 5 mg. given by intramuscular injection twice weekly, to a total of five injections.

Treatment of Symptoms of the Menopause.—The menopause is the time when the menstrual cycle ceases; it is accompanied in the majority of women by symptoms varying in severity. The commonest disturbance is the occurrence of hot flushes in which the subject suddenly becomes very red, has palpitations and breaks out into sudden perspiration. The cause of these symptoms is not known for certain, and may be either a diminution in the amount of œstrogenic substances or it may be an increased secretion of gonadotrophic hormone by the anterior lobe of the pituitary body, since some evidence indicates that the symptoms increase in parallel with the appearance of the gonadotrophic hormone in large amounts in the urine. Apparently in a normal subject before the menopause, the secretion of œstrogenic substances by the ovary inhibits excessive activity on the part of the anterior lobe. Whatever be the cause of the menopausal symptoms it is agreed that the administration of an œstrogenic substance has a beneficial effect on them. Œstrone is first given by mouth in tablets containing 0·1 to 1·0 mg. daily, and the effect on the number of hot flushes per day is observed. The dose is increased if necessary until the attacks are reduced to one or two in the day.

Androgenic Substances.—If the testes are removed from a young cockerel, so that it becomes a capon, the comb atrophies. Extracts of the testes were first prepared by Gallagher and Koch which when injected into capons caused growth of the comb. Extracts of urine, from both males and females, have also been found to produce growth of the comb. All substances which can cause comb growth are known as androgenic substances. The active hormone of the testis has been isolated as testosterone, and one of the substances in urine is androsterone. In castrated rats, the secondary sexual organs, such as the prostate and the seminal vesicles, undergo atrophy. Both testosterone and androsterone when injected can cause growth of the prostate, but testosterone alone causes a corresponding growth of the seminal vesicles.

Testosterone has been used with success in men castrated by gunshot wounds. It is injected in oily solution as the propionate, the dose being about 25 mg. given twice weekly.

If the dose is too large there is erection of the penis for long periods. After castration the prostate and seminal vesicles become atrophic and the man becomes impotent. When testosterone propionate is injected, the prostate, seminal vesicles and penis grow, and the capacity to perform the sexual act is fully restored, though it is of course sterile. Testosterone propionate has also been tried in the disease of prostatic enlargement. The theory underlying the trial was that prostatic enlargement in elderly men was caused by œstrogenic substances formed in the body by a testis which had become senile and which was no longer producing a normal amount of testosterone. It has been shown experimentally that the injection of œstrogenic substances will actually cause prostatic enlargement, and this enlargement can be prevented by the administration of testosterone. Unfortunately the clinical trials of testosterone propionate in prostatic enlargement have so far had little successs.

CHAPTER V

ACTION OF CHOLINE COMPOUNDS AND HISTAMINE

Acetylcholine.—The action of acetylcholine has been described as being twofold, like muscarine and like nicotine. When a small dose, about 2 microgrammes, is injected intravenously into an anæsthetized cat, a transitory fall of blood pressure occurs due to a dilatation of the arterioles. If a larger dose, about 40 microgrammes, is injected, the fall of blood pressure is sudden because cardiac inhibition is produced in addition to the arteriolar dilatation. These effects are abolished if a dose of atropine is injected. If, however, after giving atropine, a large dose of acetylcholine is injected, e.g. 1 mg., a sharp rise of blood pressure occurs due to the stimulation of the cells of the sympathetic ganglia which discharge impulses along the post-ganglionic fibres and constrict the blood vessels, and also due to the stimulation of the medulla of the suprarenal gland with a consequent release of adrenaline.

Now nicotine has a similar effect, but when repeated doses of nicotine are given the effect disappears as the ganglia become paralysed. When paralysis has been produced by nicotine, the injection of acetylcholine is then without effect. The effects of acetylcholine observed before the injection of atropine are muscarine-like actions, while those observed after the injection of atropine are nicotine-like.

Carbachol.—Acetylcholine is very rapidly destroyed in the body and therefore not used therapeutically. A more stable ester of choline is carbaminoylcholine, now introduced into the Pharmacopœia under the name of carbachol and formerly known as Doryl. It has been found of great use in treating retention of urine after childbirth.

Eserine or Physostigmine.—This substance inhibits the enzyme present in the blood and tissues which breaks down acetylcholine, and therefore its action in the body prolongs the life of molecules of acetylcholine set free within the body, and the effect of injecting eserine resembles the effect of giving a small continuous infusion of acetylcholine. The intestinal movements are increased, and this effect is used in the treatment of paralytic ileus. When physostigmine is put in the eye the pupil is constricted ; likewise the ciliary muscle contracts and the outlet for the aqueous humour through the canal of Schlemm is widened so that the intra-ocular pressure falls. Use of this effect is made in treating glaucoma in which the intra-ocular pressure is raised. As a further result of the contraction of the ciliary muscle, the suspensory ligament is relaxed, the lens becomes more spherical and distant objects can no longer be seen. The constriction of the pupil by physostigmine does not occur when the ciliary ganglion is removed and the nerve fibres to the sphincter have degenerated.

Histamine.—Histamine is a substance with actions which are of considerable importance, since the liberation of histamine in the body appears to be the cause of anaphylactic shock. Histamine causes contraction of smooth muscle ; thus it causes constriction of the bronchioles, and death in the guinea-pig from anaphylactic shock is due to this action. Likewise histamine causes contraction of the muscle of the uterus, and of the intestine, and in the anæsthetized rabbit histamine causes a rise of blood pressure by its action on the smooth

muscle of the blood vessels. These effects so far are consistent with one another. When, however, histamine is injected into the cat or the dog it causes a fall of blood pressure, transient after small doses and prolonged after large doses. This fall is not due to any weakening of the heart, for on isolated cardiac tissue histamine has a slight stimulant effect, and in addition it dilates the coronary vessels of the cat's heart. The fall of blood pressure is due to a dilatation of the small blood vessels, especially the capillaries, and this occurs to such an extent that in the cat histamine shock is seen in which, although the heart beats vigorously, the blood pressure is very low and the pulse pressure in the large arteries disappears. The intestines when exposed are a dusky plum colour.

Large doses of histamine kill the rabbit by producing pulmonary vasoconstriction; they kill the dog by causing stasis of blood in the liver due to contraction of the muscle surrounding the outlet of the heptatic veins into the vena carva. These effects in the rabbit and the dog are also the causes of death from anaphylactic shock in these respective species. In man histamine is used to produce a flow of gastric juice, which follows subcutaneous injection.

CHAPTER VI

THE USE OF VITAMINS IN MEDICINE

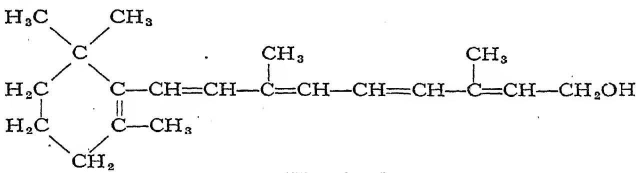
By H. M. Sinclair, D.M.

MAN'S first experiments with food were selection based on pleasing sight, smell and taste, and harmless consequences. Apart from the art of cooking, progress was at first empirical, when it was noticed that inclusion of certain substances in a diet cured or even prevented certain diseases, particularly during long sea voyages. It is only in the last half-century that the selection of food has become a science. Over fifty years ago Lunin clearly recognized that small quantities of unknown substances were essential to life; at the beginning of this century, Pekelharing demonstrated in animals the existence of disorders due to dietary deficiency, and Hopkins

first realized the full significance of vitamins. Vitamins are organic chemical compounds necessary in very small amounts for maintaining the health of an organism. This definition must be qualified by specifically excluding essential aminoacids, some of which are required in smaller daily amounts than are some vitamins. Little is known of the therapeutics of essential aminoacids in man.

Vitamin A

The beneficial effect of cod-liver oil on night-blindness, rickets and osteomalacia has been known for a long time, but it was not until 1913 that McCollum and Davis, and Osborne and Mendel proved by animal experiments that some fats contained factors essential for nutrition whereas others did not. Fractionation of fish liver oils led finally to the isolation of vitamin A, which was shown by Karrer (1931) to have the following structure :



Vitamin A

This compound has been prepared synthetically. It is colourless but is closely related to the carotenoids, a class of pigments widely distributed in nature and responsible for the colour of buttercups, tomatoes and lobsters.

Four of these compounds (" provitamins ") exhibit vitamin A activity because they can be converted into the vitamin in the body. The part of the molecule containing the ring comprises β-ionone which is of great biological importance ; the four precursors of vitamin A all contain this ring and the most widely distributed of them, β-carotene, contains two such rings in its molecule and gives rise to two molecules of vitamin A in the body. There is no doubt that this ring is essential for biological activity. Two other facts about the molecule deserve attention. First, it is an aliphatic primary

alcohol and therefore can become esterified by fatty acids, bile acids or proteins ; it is probably absorbed from the gut mainly in combination with bile acids, and transported in lymph and blood and stored in the liver in combination with fatty acids and possibly also protein. Visual purple is a compound of vitamin A with a protein, and the extremely interesting carotenoid pigment of lobsters, salmon and shrimps (called astacin) also exists in nature combined with protein. Secondly, the molecule contains five unsaturated bonds. Hydrogenation of all the double bonds results in loss of biological activity, but some of those in the side chain can be eliminated without loss of activity ; these latter bonds may be important in allowing the vitamin to function as an oxidation-reduction catalyst.

The double bonds also render the molecule liable to oxidation, and this is the commonest cause of destruction, particularly when foods are dried or dehydrated ; hay dried in the usual way in the sun contains practically no vitamin. But the ordinary methods of cooking or preserving food cause little destruction.

Morton and his colleagues have described a vitamin A_2 which can be distinguished from vitamin A by its ultraviolet absorption spectrum and by the antimony trichloride colour test. Whereas salt-water fish form predominantly vitamin A from carotene, fresh-water fish form vitamin A_2. The latter only occurs in birds and mammals if fresh-water fish are eaten.

Vitamin A can be assayed by three different methods : by feeding tests on growing rats, by a colour reaction with antimony trichloride or by a spectrographic method. Feeding tests, unlike the other two, measure both vitamin and provitamins ; the spectrographic method is the most accurate. Unfortunately, different units are used in each method. One international unit (I.U.) corresponds to the biological activity of 0·6 microgram of pure β-carotene ; it is roughly equivalent to 0·7 Sherman unit (rat feeding test) and 0·03 to 0·05 Lovibond blue unit (antimony trichloride test).

The most important sources of the vitamin or provitamins in the diet are milk, butter or fortified margarine, egg yolk, liver, green vegetables and carrots. The minimum daily requirement of an adult is about 30 I.U. per kilogram of body weight ; a value of about 50 is a safe figure to take in calculating dietary allowances ; on the basis of this figure, sufficient

for an adult is contained in a glass of milk, an egg, 25 gm. of butter and a moderate helping of green vegetables. Little is known about the factors affecting the requirement of vitamin A; it is readily absorbed from the gut, but its absorption is probably decreased in some cases of steatorrhœa and in infections. Some vitamin A but no carotene is absorbed in absence of bile. For children between the ages of two and fourteen years and for pregnant or nursing women the milk should be doubled and a teaspoonful of cod-liver oil given daily. This is important since many children in England probably consume suboptimal amounts of the vitamin, and since the requirement during pregnancy is increased. The vitamin is stored in the liver, but in new-born babies the liver contains very little ; particular attention should therefore be paid to these, more especially to premature or artificially fed infants. Large amounts can be stored : a rat can store enough vitamin A in its liver in a few days to last it for several months. 95 per cent. of the vitamin in the body is found in the liver ; as much as 1 per cent. of the weight of halibut livers may be vitamin A. Transformation of carotene to vitamin A occurs in the liver, and in diseases of this organ or in diabetes mellitus this transformation is decreased and large quantities of carotene appear in the blood ; in cirrhosis of the liver increased amounts of vitamin A are also excreted in the urine.

Nutritive Functions.—In absence of vitamin A atrophy of epithelial tissues and also night-blindness occur.

The earliest symptom or sign of deficiency is usually poor dark adaptation (hemeralopia). This can be measured photometrically, and subnormal values are not uncommon in apparently healthy people in this country ; but only about half these values revert to normal upon therapy with vitamin A, the other half being caused by factors other than deficiency. The importance of night-blindness in relation to traffic accidents, particularly in the "black-out," is obvious. The part played by the vitamin in dark adaptation has been elucidated by Wald and others. The rods of the retina are sensitive only to intensity of light and are especially adapted to function in dim light. They contain visual purple (rhodopsin) which is converted by light into visual yellow with initiation of nerve impulses. In absence of light, visual yellow returns into visual purple. The latter, as already mentioned,

is a conjugated protein in which vitamin A is the prosthetic group. In deficiency of the vitamin there is a decreased amount of visual purple and so night-blindness results.

Changes in epithelial tissues resulting from vitamin A deficiency are atrophy of the cells and reparative proliferation of basal cells followed by differentiation into a stratified keratinizing epithelium which is identical wherever produced and comparable in all its layers with epidermis. In animals the changes occur first in the trachea and bronchi, next in the pelvis of the kidney, later in the eyes, pancreas, ureters gonads and elsewhere; masses of keratinized epithelial cells may block the bronchioles, giving rise to bronchiectasis, atelectasis and pneumonia; keratinization of the cornea and conjunctiva leads to xerophthalmia; atrophy of the enamel-forming epithelium of teeth causes the formation of enamel to cease, and marked deformities occur as a result of defective formation of dentine. Clinically, epithelial changes occur mainly in the conjunctivæ and skin. The conjunctiva becomes opaque and the deeper vessels become invisible; wrinkling and dryness may appear, and finally characteristic Bitôt's spots are seen. These are foamy, white patches, usually triangular and situated just outside the limbus; they are superficial and not wetted by tears, and they must not be confused with pinqueculæ. In the skin there is hyperkeratosis of the hair follicles, particularly over the triceps area; the skin is dry and rough, and there is atrophy of the sweat glands. In humans with deficiency of vitamin A, nerve lesions have not been reported; but E. Mellanby found degeneration of the myelin sheaths in the spinal cord, particularly in the sensory tracts, in dogs, and he and M. Mellanby have suggested that loss of neurotrophic control owing to vitamin A deficiency may be responsible for the epithelial changes and dental caries. More recently, he has found that the deafness that occurs in animals on a diet deficient in vitamin A is due to hypertrophy of bone squeezing the eighth nerve, and not to a primary effect of the deficiency on the nerve as at first thought. Bessey and Wolbach have concluded that "there is no substantial evidence that degeneration of myelin sheaths is a specific consequence of vitamin A deficiency." Since epithelial metaplasia invariably follows deficiency of vitamin A, it is difficult to believe that loss of neurotrophic control causes the epithelial changes. It is tempting to believe that vitamin A

is concerned in the metabolism of epithelial tissues, and that the changes that occur in deficiency are due to a faulty metabolism.

Deficiency may be assessed by estimating vitamin A in plasma, or by estimating dark-adaptation photometrically.

Therapeutic Uses.—Severe deficiency with Bitôt's spots or xerophthalmia is rare, but occasionally occurs in this country and should be treated with large doses of vitamin A. Patients who complain of night-blindness or glare-blindness, and who show clinical signs of deficiency or deficient dark adaptation by photometry, should receive supplements of the vitamin.

In cases of infection, particularly of the respiratory tract, a careful dietary history should be taken, and in cases of steatorrhœa secondary deficiency of vitamin A should be suspected. As already stated, infants and pregnant or nursing women should be given additional amounts of the vitamin. The epithelial changes respond rapidly to therapy, and hemeralopia, if due to deficiency, is quickly abolished, sometimes within a few hours. Vitamin A has been claimed to be valuable in the treatment of Darier's disease, pityriasis rubra pilaris and in senile vaginitis. It increases resistance to infection only in presence of deficiency, and there is no justification of its use as a prophylactic against colds and influenza if the diet is adequate. There is no evidence that it prevents renal calculi, or exerts a good effect in thyrotoxicosis, demyelination of the spinal cord or anæmia; it is no more important in contributing to normal growth than any one of the other vitamins, essential aminoacids or salts.

Many good preparations of fish-liver oils are available. *Oleum Morrhuæ* (B.P.) has a slightly fishy taste; the prophylactic dose is 1 to 2 mils t.d.s. and the therapeutic dose 3 to 6 mils t.d.s. 1 gm. contains not less than 600 I.U. vitamin A and 85 I.U. vitamin D. Halibut-liver oil is fifty to one hundred times as potent and is more pleasant to take, but contains less vitamin D in a dose. A suitable dose is 5 to 10 drops daily for infants, and for adults this may be doubled; the curative dose is 10,000 to 40,000 I.U. daily. Excessive administration of vitamin A to animals has been reported to damage bone, kidneys and skin, but there are no dangers involved in using the usual liver oils even in high doses. Large doses of carotene given orally or by injection are harmless.

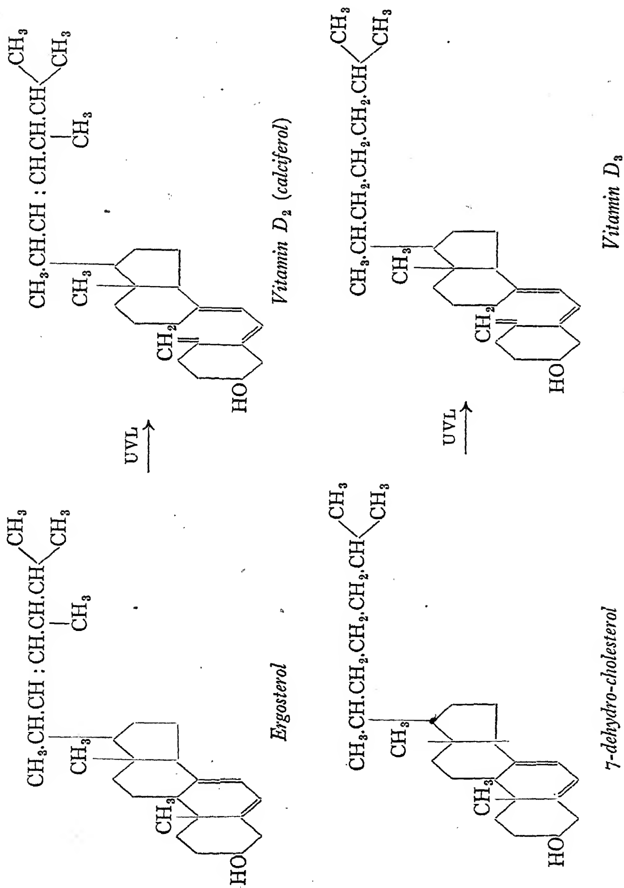
Vitamin D

The work of Mellanby, McCollum, Hess and Steenbock laid the foundations of our knowledge of vitamin D, and a compound with antirachitic activity was isolated in pure crystalline form in 1931. It was soon found that there were several chemically distinct forms of vitamin D, and at present at least ten are known. All are sterol derivatives. In 1932 Rosenheim and King introduced the new formula for sterols, showing that they were derived from *cyclo*pentenophenanthrene. Vitamins D therefore are chemically related to cholesterol, the sex hormones, the adrenal cortical hormones, certain carcinogenic compounds, certain toad poisons, cardiac glucosides, and embryological organizers. Only two forms of vitamin D are known to be important in medicine, calciferol (vitamin D_2) and vitamin D_3 (there is no vitamin D_1, as this term was applied to what proved to be a mixture). These two compounds are formed from inactive provitamins by the action of ultraviolet light. The provitamin of calciferol is ergosterol, which is the characteristic sterol of yeast and fungi; the provitamin of vitamin D_3 is 7-dehydro-cholesterol which is present in animal fats, fish oils, eggs and milk.

The conversion of provitamin to vitamin takes place in the body if the skin is exposed to ultraviolet light. The change of ergosterol into calciferol is a photochemical reaction initiated by any wave-length of light absorbed by ergosterol; the change is merely a re-arrangement within the molecule, and no atoms are lost or gained.

Vitamin D_3 has the same antirachitic potency as calciferol in rats, but is very much more effective in chickens. The remarkable specificity of antirachitic activity is illustrated by the fact that 7-dehydro-stigmasterol, which differs from ergosterol only in having an ethyl instead of a methyl group at C_{24} in the sidechain, has no activity after irradiation.

Vitamin D is assayed by the "line test" which depends upon the fact that under properly controlled conditions the degree of healing in the bones of rachitic rats is proportional to the amount of vitamin D administered. The international unit is defined as the vitamin D activity of 1 mg. of the international standard solution of irradiated ergosterol, which has been found equal to that of 0·025 μgm. of crystalline vitamin D. Natural foods containing vitamin D are of animal origin.


Ergosterol
UVL
Vitamin D_2 (calciferol)
7-dehydro-cholesterol
UVL
Vitamin D_3

Fish that contain much body-oil, such as sardines and herring, are the richest sources ; eggs are next in importance and followed by milk, butter and liver. But it is insufficiently realized that the amounts present in eggs, milk and butter are very small, and by themselves inadequate to supply children with vitamin D. One egg contains 20 to 60 I.U., a pint of summer milk about 20 I.U. (but milk from cows kept indoors contains practically none), and a pat of butter (10 gm.) about 8 I.U.

About 400 I.U. a day are required by infants to prevent the onset of rickets and to promote optimum skeletal growth and dentition. Premature babies may require twice as much. It is obvious, therefore, that infants should receive supplements of vitamin D. Little is known about the requirements of children or adults, but they are probably of the order of 400 I.U. a day. During lactation, about 600 I.U. are required.

Nutritive Functions.—Rickets is due to a fault in the metabolism of calcium and phosphorus, and vitamin D prevents or cures rickets by causing the correct amounts of these salts to be present in the body fluids. Bone is laid down only in presence of adequate amounts of $Ca^{\cdot\cdot}$, PO_4''' and CO_3'', and rickets may result from diets low in calcium or low in phosphorus ; not only the absolute amount of each, but also the ratio of one to the other determine the rachitogenic properties of a diet, because increasing one salt produces deficient utilization of the other. The acid-base content of the diet also affects the two salts ; rachitogenic diets have been converted to normal by addition of organic acids and alkaline ash, and normal diets may be made rachitogenic by adding alkalis and acid ash. Vitamin D acts mainly by increasing the absorption of calcium in the small intestine ; it therefore raises blood calcium if the diet contains calcium salts. The parathyroid hormone also raises blood calcium, but by withdrawing calcium from the bones. Their actions are independent : whereas excess vitamin D causes hypercalcification, excess parathormone causes decalcification. A relation between dental caries and absence of vitamin D has been claimed by M. Mellanby. In fatty diarrhœas, insoluble calcium soaps are produced and the absorption of calcium is diminished. Diminished absorption also occurs if the diet contains certain cereals that contain phytic acid which pre-

cipitates calcium in the gut and so prevents absorption. Since wheat contains this substance, it is very desirable to add calcium to bread, but unfortunately the small amount that is being added is only just sufficient to neutralize the phytic acid.

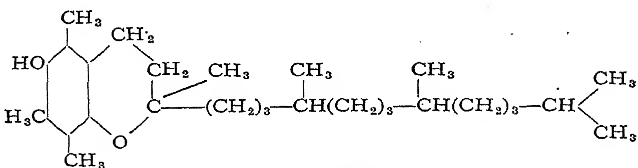
Therapeutic Uses.—Greatest susceptibility to rickets occurs during the first months of life, and as milk is a poor source of vitamin D, infants should receive supplements, as stated above. Infants tolerate cod-liver oil concentrates well, and one-half or one teaspoonful of *Oleum Morrhuæ* (B.P.) daily provides about 200 or 400 I.U. After about the second month, two or three teaspoonfuls may be given daily throughout the first year, and halved during the second year. The dose may be decreased during the summer, and the preparation stopped if vomiting is frequent because of the possibility of lipoid pneumonia being produced by aspiration. For premature infants requiring 1000 to 10,000 I.U., or for children who do not tolerate cod-liver oil, more concentrated preparations may be used. *Liquor Calciferolis* (B.P.) contains 3000 I.U. per gm. The daily prophylactic dose for an infant is stated as 1000 to 2000 I.U. (0·3 to 0·6 mil) and the therapeutic dose 2000 to 3000 I.U. (0·6 to 1 mil). This preparation, unlike cod-liver oil, contains no vitamin A. In treatment of rickets doses of 5000 to 10,000 I.U. are usually sufficient, but occasionally the dose may have to be raised to 30,000 or more. Very rarely refractory cases are found: the case is described of a boy 16 years old in whom rickets persisted until over a million units were given daily, and then 150,000 units daily were necessary to maintain the normal state. If very large doses (100,000 I.U. or more daily) are given, the urine should be examined daily for calcium casts, the serum calcium should be estimated weekly (it should not rise above 12 mg. per 100 mil), and X-ray examinations of the bones made at intervals. As long as the calcium and inorganic phosphorus levels in the blood are not raised above normal, there is no danger. Toxic doses produce a rise in calcium and metastatic calcification occurs; there are also symptoms such as nausea, anorexia, headache, lassitude and frequency of micturition.

Supplements of the vitamin should possibly be continued during the growing period, particularly as there is evidence that vitamin D lessens the incidence of caries. The requirements during adolescence and adult life are not known; but

about 800 I.U. daily should be administered during pregnancy and lactation, and invalids confined indoors and night workers might need supplements.

Vitamin E

In 1922 Evans and Bishop found that on supposedly complete diets, and with both growth and external appearance normal, rats could have normal œstrus cycles and would breed, ovulate and conceive, yet be unable to have a normal gestation because the fœtus invariably died. Evans announced the existence of a new vitamin, and his work was quickly confirmed. Recent extensive researches in his laboratory into the chemistry of vitamin E have led to the recognition of a group of active compounds named tocopherols, and Evans and his colleagues have crystallized some derivatives of these. In 1938 Karrer announced the synthesis of α-tocopherol, the most active form of vitamin E:



α-tocopherol

Vitamin E is readily oxidized, particularly in presence of fats. It is present in vegetable oils, especially wheat-germ oil. The usual method of assay uses adult female rats fed on a diet deficient in the vitamin; if the dose be inadequate the embryos die and are absorbed, but with adequate amounts living young are born.

The lesion in vitamin E deficiency occurs in the embryo in the female and is curable, and in the testis in the male where it is irreparable. The embryo is apparently normal until the tenth day, when probably cell proliferation in the mesoderm blocks the blood vessels of the blastoderm and the embryo dies of anæmia. Mason has studied the lesion in the testis in the male in deficiency of vitamin E and contrasted it with testicular degeneration produced by deficiency of vita-

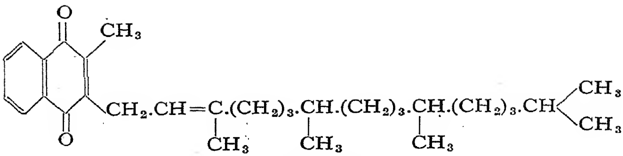
min A. Deficiency of E produces excessive liquefaction of the chromatin material, at first in the spermatozoa and spermatids and later in less mature cells; spermatogenic activity ceases early, whereas in deficiency of vitamin A it continues despite considerable loss of germinal epithelium. Mason concludes that vitamin E plays an essential part in nuclear activities involving chromatin and is particularly indispensable in those tissues in which cellular proliferation and differentiation are unusually rapid (such as the testis in the male and developing embryo in the female).

The functions of vitamin E appear not to be confined to reproduction. In its absence young rats fail to grow at the normal rate and may develop paralysis of the hind limbs. Also suckling rats from mothers deficient in vitamin E develop extensive degeneration and necrosis of muscles, which is prevented but not cured by administration of the vitamin.

What relation this work on lower animals bears to disease in man is unknown. Several authors have reported dramatic results in cases of threatened or habitual abortion, and in various neuromuscular disorders (such as amyotrophic lateral sclerosis and progressive muscular atrophy). At the present time, there seems insufficient evidence to conclude that in humans the vitamin may prevent sterility in the male or muscular dystrophy.

Vitamin K

In 1929 and subsequently Dam showed that a fat-soluble vitamin existed that prevented the appearance of a hæmorrhagic disease in fowls. The disease is characterized by a great tendency to hæmorrhages and a diminished clotting power of the blood, due to a reduction in the amount of prothrombin. Later it was produced in other animals and the factor concerned in preventing it was called vitamin K. It is present in green vegetables, tomatoes and liver. Two natural forms of the vitamin, K_1 and K_2, have been isolated, one from alfalfa and the other from fish meal. Several artificial forms have been synthetized, and one is water-soluble; one artificial form, 2-methyl-1,4-naphthoquinone, is more active than the natural forms. Vitamin K_1 has the following formula:



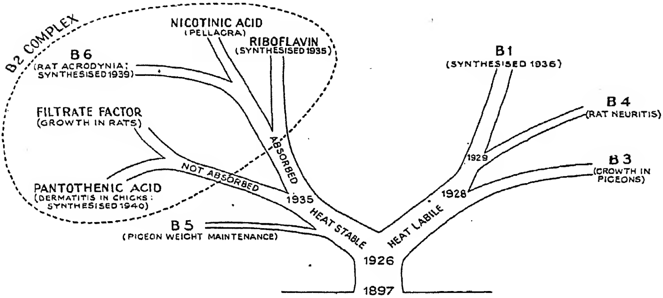
Vitamin K_1

In patients or animals with obstructive jaundice or biliary fistulæ, a hæmorrhagic diathesis may develop, the amount of prothrombin in the blood may be low, and the hæmorrhagic tendency may be corrected by vitamin K therapy. Bile is necessary for the absorption of this vitamin from the gut, and in the adult synthesis in the gut occurs through bacterial action. Deficiency is also apt to arise in pregnancy, partly because the requirement is increased, and partly because of the prevalent use of liquid paraffin which prevents absorption of the vitamin. Excellent results from therapy have been obtained in hæmorrhagic disease of the newborn.

Vitamin B Complex

The term "water-soluble B" was originally used for the antineuritic vitamin discovered by Eijkman in 1897. Vitamin B_2 was distinguished in 1926 as a factor that prevented pellagra and was more stable to heat than vitamin B_1. Two years later B_3 was recognized as a factor necessary for growth in pigeons adequately supplied with B_1 and B_2; and B_4 was shortly believed to be a factor that prevented the development in rats of a hunched back, incoordination and red swollen paws. B_5 arrived in 1930 and permitted maintenance of weight in pigeons. Vitamins B_3, B_4, and B_5, as well as several other factors (such as the "anti-gizzard-erosion factor for chicks" described by Bird *et al.*) are not known to have any clinical significance and will not be further considered here, but attention must be paid to the subdivision of vitamin B_2. Rats fed on a diet deficient in this vitamin failed to grow and developed a dermatitis, and this was believed to be analogous to pellagra. When the fluorescent compounds called flavins were discovered in 1933 it was found that one of these (ribo-

flavin) could be isolated from preparations of vitamin B_2 and would promote growth in rats adequately provided with

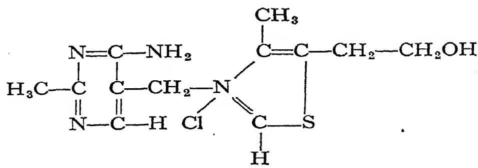


Vitamin B

vitamins B_1, B_4, and B_6. But pure riboflavin was found to have no effect upon this dermatitis of rats or upon human pellagra; it was obvious therefore that vitamin B_2 must consist of more than one factor. In 1935 it was shown that the factor that prevented rat dermatitis was vitamin B_6, and so for the rat vitamin B_2 consisted of riboflavin and B_6. But neither of these components, either alone or in combination, cured human pellagra, and therefore the original "vitamin B_2" consisted of at least three factors: riboflavin, vitamin B_6, and the pellagra-preventive factor now identified as nicotinic acid. These factors are all adsorbed on fuller's earth, but there are two other factors, necessary respectively for the growth of rats and prevention of dermatitis in chicks, that are not adsorbed; one is called the "filtrate factor" and the other is pantothenic acid; these five factors compose the vitamin B_2 complex.

Vitamin B_1 (thiamin)

Chemical work done in various laboratories led finally to the synthesis of vitamin B_1 in 1936. The molecule contains a pyrimidine and a thiazole ring:



Vitamin B_1

The vitamin withstands boiling in acid medium, but is destroyed in neutral or alkaline solution. Considerable destruction takes place when foods are tinned. It is assayed by growth or curative tests in animals; by oxidation to thiochrome, a product that gives a blue fluorescence that can be estimated; or by a colour reaction. The international unit is equal to 3 μgm. of synthetic vitamin B_1.

There are few common foods that are rich in the vitamin. Wholemeal bread is a good source, containing about ten times as much as white bread and twice as much as brown; National Wheatmeal bread contains about 330 μgm./100 gm. Oatmeal, liver, kidney, peas, broad beans and nuts, oysters and egg yolk are all good sources, but milk is rather poor and beer contains little. The minimum required to prevent symptoms of beriberi in an adult man is not less than 0·5 mg. a day, and the optimum intake is about 2 mg. Many factors, however, alter the requirement. It is proportional to the body weight, the total metabolism, and the energy value of the ingested carbohydrate. Anything that increases metabolism, such as muscular work, fever, pregnancy, or hyperthyroidism, increases the amount of the vitamin required. The vitamin is necessary for the oxidation of carbohydrate and for its conversion to fat. A diet high in fat has a sparing action on vitamin B_1; but beriberi has sometimes followed diets very high in carbohydrate and otherwise normal, and "alcoholic" polyneuritis is caused by the ingestion of diets high in calories (as alcohol) but low in vitamin B_1. Failure to assimilate the vitamin may also cause deficiency, and includes both failure of absorption from, and destruction in, the gut. In some cases of disorders of the gut—for instance, patients with chronic diarrhœa or achlorhydria—deficiency may occur

probably through failure of absorption; in achlorhydria destruction also occurs because the vitamin is unstable in alkali; and it is destroyed even in an acid medium in presence of hæmin (for instance in gastric ulcer or gastric carcinoma). There is very little storage of the vitamin in the body.

Nutritive Functions.—The earliest symptoms of deficiency are loss of appetite and muscular weakness; later there is tenderness of the calf-muscles, loss of reflexes and vibration-sense in the legs, and hyperæsthesia followed by anæsthesia advancing up the legs. The arms are affected later. The cardiovascular changes include dyspnœa, tachycardia, and dilatation of the heart; there is peripheral vasodilatation, and œdema which may be mild or extreme. Dry and wet beriberi; "alcoholic," gastrogenous and nutritional polyneuritis; and possibly some cases of polyneuritis of pregnancy and of diabetes are all due to deficiency of vitamin B_1. Recent work has shown that subjects placed upon diets low in vitamin B_1 develop diminished physical and mental efficiency, and neurasthenia.

The way in which the vitamin acts in the body has been worked out mainly by Peters. Using pigeons and rats, he has shown that in deficiency lactic and pyruvic acids accumulate in the body because they are formed from carbohydrate but cannot be further broken down. Avitaminous brain tissue *in vitro* is unable to oxidize pyruvic acid but does so when minute amounts of B_1 are added; normal tissue oxidizes pyruvic acid and is unaffected by additional B_1. It therefore seems that vitamin B_1 is necessary for the oxidation of pyruvic acid in the body:

$$\text{Glucose} \longrightarrow \text{Lactic acid} \xrightarrow{+O} \text{Pyruvic acid} \underset{\substack{\uparrow \\ \text{vitamin } B_1}}{\xrightarrow{+O}} \text{Acetic acid} + CO_2$$

This work on lower animals has been confirmed by the study of patients with beriberi, and it goes far towards explaining the symptoms. The biochemical change occurs particularly in nerve cells and in the heart, producing by disordered metabolism the peripheral neuritis and cardiac symptoms.

Lohmann showed that the coenzyme "cocarboxylase" (which catalyses the breakdown of pyruvic acid in yeast) is

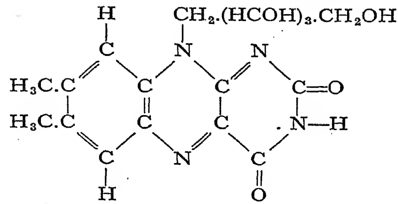
vitamin B_1 combined with two phosphate molecules. It is now certain that the vitamin must be converted to the diphosphate before it acts in the body, and this phosphorylation takes place in liver, kidney and nucleated cells derived from reticuloendothelial tissue.

As the amounts of free vitamin and of cocarboxylase in blood are very small, it is difficult to estimate deficiency by assay of the vitamin in blood. An estimate of both can, however, be obtained by a modification of Schopfer's method (which consists of growing a fungus upon the blood) and of cocarboxylase alone by a modification of Lohmann's method (which measures its activity in presence of excess carboxylase and pyruvic acid). In urine the vitamin may be estimated by oxidation to thiochrome and estimation of fluorescence.

Pure vitamin B_1 is now readily available for therapeutic use, either orally or parenterally. In beriberi, and in neuritis or cardiac dilatation, accompanied by alcoholism, pregnancy, infections, disorders of the gut, diabetes, idiopathic hypochromic anæmia or hyperthyroidism, and in anorexia, it is wise to start treatment with intramuscular or intravenous injection of from 20 to 50 mg. daily. Later the same dose may be given orally, or the injections decreased to 10 mg. daily. Care should be taken in cases of pregnancy, fevers, diets for gastric ulcers or glucose for ailing infants, to ensure that adequate vitamin B_1 is included in the diet. Dried powdered brewers' yeast is a convenient source of the vitamin B complex; it is easily administered stirred into milk, or in warm water with salt, and about 30 gm. daily is a convenient dose for an adult. *Pulvis Vitamini B_1* (B.P.) contains 100 I.U. (0·3 mg.) per gm.; the daily prophylactic dose is 1 to 2 gm., and the therapeutic dose 2 to 6 gm. The latter however is probably five times too small, since there is evidence that the best results are obtained with massive therapy. There is no danger of overdosage or cumulative toxic effects; intravenous administration of 100 mg. is without untoward effects and is about $\frac{1}{360}$th of the toxic dose.

Riboflavin.

Riboflavin is necessary for various animals, including man; it has been synthesized and has the following formula:



Riboflavin

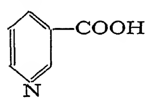
It prevents certain disorders in rats (such as conjunctivitis, alopecia, cataract, and even pediculosis), and dermatitis in turkeys. The work of Sebrell and Sydenstricker has shown that deficiency of riboflavin in man produces a fourfold syndrome. First, there is a superficial symmetrical vascularizing keratitis; the capillaries at the limbus pass beyond the scleral digitations and invade the cornea just beneath the epithelium; in marked deficiency, corneal opacities occur. This is accompanied by photophobia, burning and itching of the eyes. Secondly, the papillæ of the tongue become denuded and their capillaries congested, giving a smooth magenta-coloured glossitis. Thirdly, there is denudation of the lip mucosa along the line of closure (cheilosis), and also transverse fissures at the muco-cutaneous junction in the corners of the mouth (angular stomatitis). Fourthly, there is a wet seborrhœic dermatitis affecting particularly the nasolabial folds, the alæ nasi, the inner canthi, the ears, and later the limbs. These signs disappear upon therapy with the vitamin, the glossitis in three or four days, and the keratitis in about a week. Good results with riboflavin therapy have been claimed in syphilitic and in rosacea keratitis.

The daily requirement of riboflavin is probably 2·5 mgm., and the therapeutic dose 6 to 15 mgm. orally or by injection. There are no toxic effects. The main dietary sources are milk, liver, egg-yolk, meat, green vegetables, and wholemeal (or National Wheatmeal) bread. Like vitamin B_1, riboflavin acts in the body combined with phosphate; and riboflavin phosphate in combination with protein forms a factor (sometimes called the "yellow emzyme") that was shown by Warburg to be very important in cell respiration. Verzár believes that fatty acids are imperfectly absorbed from the gut

in absence of riboflavin phosphate, and suggests that cases of idiopathic steatorrhœa, sprue and cœliac disease should be treated with it.

Nicotinic Acid (*niacin*).

Pellagra is rare in this country, and is seldom recognized when it does occur. The symptoms may be summarized as weakness and lassitude, anorexia, diarrhœa, sore ulcerated mouth of a fiery red, mental changes and typical cutaneous lesions. These latter consist of a very characteristic dermatitis on the exposed surfaces, of lesions about the genitalia, seborrhœa on the face and neck, and hyperkeratoses over bony prominences. The glossitis of nicotinic acid deficiency differs from that caused by deficiency of riboflavin in that in the former the capillaries of the flattened papillæ are dilated and contain arterial blood, giving a bright red colour rather than the congested appearance of the latter. The story of the discovery of the factor preventing it may briefly be summarized. Warburg and von Euler showed that nicotinic acid amide was an active group in two coenzymes important in cell respiration. This led to its use in other fields, and late in 1937 Elvehjem and others showed that it cured " black-tongue "—a disease in dogs analogous to pellagra. Several workers immediately tried it and certain related compounds in cases of pellagra, and there is little doubt that the disease can be completely cured by oral administration of nicotinic acid



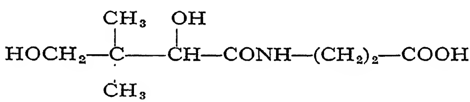
or its amide ; coramine, which is a related compound, is also effective. Pellagra is fairly common in alcohol addicts who drink spirits, and is occasionally seen in this country accompanying ulcerative colitis or other disorders of the gut.

The mental changes, which are due to the same pathological lesion as in Wernicke's encephalopathy, respond to large doses of nicotinic acid ; the peripheral neuritis responds to vitamin B_1, and the same is probably true of Korsakov's psychosis. Good results from therapy with nicotinic acid have been claimed in Vincent's angina and in some cases of simple glossitis. Nicotinic acid is cheap, and the curative dose is

150 to 300 mg. a day, given by mouth in doses of 50 mg. The dose is carefully stated because it must be emphasized that, unlike vitamin B_1, nicotinic acid is definitely toxic, large amounts producing flushing, burning and itching of the skin, and increased motility of the stomach; these effects, however, are not produced by nicotinic acid amide. The main dietary sources are meat, liver, milk, egg yolk and green vegetables. The daily requirement is probably about 20 mg. The term "niacin" has recently been adopted in the U.S.A. in place of nicotinic acid, because of the unfortunate association of the latter with nicotine; it is hoped this term will become universal.

Pantothenic Acid.

This widely distributed substance was synthesized in 1940 and shown to be α,γ-dihydroxy-β,β-dimethylbutyryl-β'-alanide:

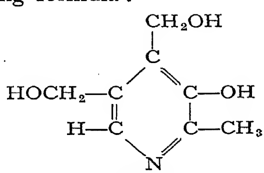


Pantothenic acid

It is alleged to be essential to human nutrition, but the signs and symptoms of deficiency in man have not yet been characterized. In animals, deficiency produces increased vascularity and then atrophy of the adrenal cortex.

Vitamin B_6 (pyridoxine).

Vitamin B_6 has been synthesized (1939) and found to have the following formula:



Vitamin B_6

Signs and symptoms of deficiency in man have not yet been characterized, but intravenous administration of 20 to 50 mg.

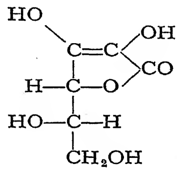
daily has been claimed to cure cheilosis associated with pellagra, sprue, and other diseases associated with gastro-intestinal disturbances. In rats it prevents a symmetrical dermatitis that is called " rat acrodynia " because it is alleged to resemble pink disease in children. The vitamin causes increased growth of plants, and may have a wide biological importance. It may be mentioned that pink disease is believed by many to be a deficiency disease. There is as yet little evidence in favour of this view, and it seems rather more probable that the primary cause will prove to be a virus. The pink colour of the skin of the hands and feet in children with acrodynia is due to capillary dilatation, and the same is true of the red paws of rats with deficiency of vitamin B_6 or of riboflavin. But this is a very unspecific lesion. In deficiency of vitamin A, of vitamin B_6 or of riboflavin, vascularization of the cornea occurs ; probably in each case the metabolism of the corneal cells is deranged in a specific way, and metabolic products accumulate and cause the invasion of capillaries. Both vitamin B_6 and riboflavin phosphate occur in yeast, which may be administered as recommended above.

Vitamin C

The value of fruit juice in the treatment of scurvy has been known for three centuries. In 1753 Lind published his excellent *A Treatise of the Scurvy* in which it was shown that the disease could be rapidly cured by lemon juice ; and after an interval of only 42 years the Admiralty introduced this remedy as an antiscorbutic measure. Early in the eighteenth century Michael had made extensive attempts to isolate the antiscorbutic principle, but his extracts had to be sent once a year to the East Indies to be tested on cases of scurvy, and the instability of the vitamin defeated him ; he found, however, that an oil-extract of scurvy grass was effective. Shortly after Lind's work, Stark twice induced scurvy in himself by careful dietetic experiments, as a result of which he died. Despite this excellent work in the field of clinical science, it was not until Holst and Fröhlich observed in 1907 that the guinea-pig could be used as an experimental animal for the study of scurvy that rapid progress was made. A similar story could be told of most of the work on vitamins, indeed of most of the great recent advances in medicine : laboratory

experiments mainly on lower animals and cautiously applied to man have rapidly increased our knowledge of the prevention and cure of disease.

In 1928 Szent-Györgyi had studied a strong reducing substance which occurred in the adrenal cortex, in cabbages and oranges. He named it "hexuronic acid" and found later (1932) that it protected against scurvy; in the same year Waugh and King showed that vitamin C isolated from lemons was identical with "hexuronic acid." A year later the vitamin, renamed "ascorbic acid," was synthesized independently by Haworth and Reichstein, and shown to have the following formula :



l-ascorbic acid

l-ascorbic acid is the most active antiscorbutic factor known and *d*-ascorbic acid is inactive ; other closely allied compounds with less activity are known. The vitamin owes its strong reducing properties to its double bond ; the compound is easily oxidized by a great many organic compounds and inorganic ions to form dehydroascorbic acid. The latter is readily reduced by glutathione, cysteine and the "fixed -SH" groups of proteins ; glutathione rapidly reduces dehydroascorbic acid *in vivo* to vitamin C.

Dehydroascorbic acid easily becomes further oxidized, and this change is irreversible. It is for this reason that vitamin C is very readily destroyed in foods during storing or cooking. Green vegetables that stand at room temperature for a few days lose half their vitamin, but cold storage protects it. Boiling a cabbage in an open vessel causes almost complete destruction. Crushing vegetables (for instance spinach or turnips) before they are cooked liberates enzymes which destroy most of the vitamin, and adding soda to make vegetables green inactivates it rapidly because it is much more easily destroyed in neutral or alkaline solution than in

acid. Further, minute traces of copper completely inactivate the vitamin in a few minutes. Good tinned foods may retain considerable vitamin C, but most commercial tinning destroys a great deal. The richest sources are black currants, oranges, lemons, grapefruit, tomatoes, raw cabbage, and rose-hips; potatoes are one of the most important dietary sources.

A pint of average commercial milk contains about 5 mg. of vitamin C; fresh raw milk contains about 14 mg. The value slowly decreases even in the cold, and is rapidly diminished by sunlight. Pasteurization usually destroys about 50 per cent., but if properly done causes only slight inactivation. Human milk is about five times richer in the vitamin than cow's milk. An infant should receive not less than 25 mg. a day; this amount just prevents scurvy in adults, who probably should receive 50 to 75 mg. a day. Primates and guinea-pigs are the only known animals that cannot synthesize vitamin C. Tissues with high metabolic activity in general contain most; the pituitary body has the highest concentration, and is followed by the adrenal cortex and corpus luteum.

Plasma contains about 1 mg. per 100 mil, and the white cells of blood about 30 mg. per 100 gm. The vitamin is readily absorbed from the normal gut, but is easily destroyed by alkali in cases of achlorhydria or by bacteria in cases of pyloric stenosis, and is absorbed with difficulty in some disorders of the gut.

Nutritive Functions.—Vitamin C is necessary for the formation of the intercellular material of tissue derived from mesenchyme. In its absence collagen is not formed between the cells of connective tissue, and osteoid tissue in bone and dentin in teeth are imperfectly formed; there is probably also deficiency of intercellular material in the endothelium of capillaries. In scurvy the main lesions are therefore found in bones (particularly at the costochondral junction), the teeth and the gums around diseased teeth, and the capillaries (causing hæmorrhages); follicular hyperkeratosis also occurs. Petechial perifollicular hæmorrhages are an early and constant sign. The Landis capillary resistance test, which is sometimes used for detecting mild deficiency, is based on this fragility of the capillaries but is of little value. Other tests have been devised. Three main biological methods of assay of the vitamin are used but, although more specific, they are more tedious and less accurate than chemical methods. The usual

method is to titrate the solution containing vitamin C against an indicator, 2,6,dichlorophenolindophenol, under controlled conditions and after eliminating interfering substances. This method has been extensively used with plasma and urine, and has recently been applied to the white cells of blood.

For therapeutic purposes, fresh orange juice (which contains about 50 mg. vitamin C per 100 mil) is admirable. It is probably advisable to give vitamin C to all babies from about the third week of life onwards, particularly to those that are fed artificially, and this may be given in the form of a teaspoonful of fresh orange juice a day, gradually increasing the dose; black currant purée and rose-hip syrup are excellent substitutes. Some infants do not tolerate fruit juice, and in these cases the crystalline vitamin may be given. *Acidum Ascorbicum* (B.P.) contains not less than 98 per cent. crystalline ascorbic acid; the daily prophylactic dose is 25 to 50 mg., and the therapeutic dose 100 to 250 mg. There is no danger of toxicity with higher doses, as 1000 to 6000 mg. have been given orally and intravenously to adults in repeated doses without harmful effects. Large doses should be used in the treatment of scurvy. Several authors have claimed that very large doses diminish the pigmentation in cases of Addison's disease.

There is no doubt that deficiency of vitamin C lowers resistance to infection and the rate of healing of fractures and wounds, but there is no evidence that it increases such resistance or healing in absence of deficiency. However, since many people in this country ingest suboptimum amounts, supplements should be given when there is a poor dietary history or low plasma values, and in chronic infectious diseases (especially tuberculosis). In pregnancy and lactation, increased amounts of the vitamin are required.

Vitamin P

Szent-Györgyi claimed in 1936 that certain flavones (plant pigments completely unrelated to flavins), in particular hesperidine and eriodictyol glucosides, cured some of the symptoms of scurvy and prevented hæmorrhages in "hæmorrhagic purpura, nephritis, sepsis, nephrosis, polyarthritis." He named the factor vitamin P. Later it was found that his vitamin acted only in presence of traces of vitamin C.

The existence of vitamin P is doubtful, but Szent-Györgyi recommends the daily intravenous injection of 25 to 200 mg. of eriodictyol glucoside in cases of hæmorrhagic diathesis and even in the treatment of acute nephritis. It should be mentioned that authors have claimed to have cured patients supposed to have scurvy and raised their serum ascorbic acid by the use of lemon juice after ascorbic acid had proved to be without effect. Recent work in Copenhagen has shown that deficiency of vitamin P can cause hæmoptysis and infiltration of the lungs simulating tuberculosis. Further clinical trials with vitamin P are necessary before a definite statement about its therapeutic use can be made.

Unsaturated Fatty Acids (Vitamin F)

In 1927 Evans and Burr found that rats fed on a diet of casein, sucrose and salts, together with vitamins A, B, D and E, developed defective ovulation and lactation. This was corrected by the addition to the diet of lard, liver or lettuce. The active principle was later shown to be unsaturated fatty acids (e.g. linoleic or linolenic acid), and it was later shown that either of these in the diet was necessary for the prevention of a scaly dermatitis in rats. The oral use of oils containing such unsaturated acids (e.g. arachis oil or linseed oil) has been advocated for many human dermatoses, and good therapeutic results have been claimed in infantile eczema and seborrhœic dermatitis.

Other Vitamins and Fatty Livers

Fatal cases of deficiency diseases are frequently found to have fatty infiltration of the liver. It has recently been shown that three vitamins are all concerned in animals with the production of fatty livers. Absence of *choline* from the diet of rats was shown by Best and others to produce this change (and also hæmorrhages in the kidneys); the reason is that choline forms part of the phospholipids made in the liver. This effect of choline deficiency can be enhanced by adding cystine to the diet or alleviated by adding methionine: choline is concerned in transmethylation, and converts cystine into methionine.

Biotin, which has been crystallized, is a growth factor for lower organisms and prevents a dermatitis in animals. It produces fatty livers by increasing fat synthesis, and this

effect can be abolished by feeding egg-white (which contains avidin—a substance that combines with biotin) or *inositol*. The latter has recently been shown to be essential for mice, deficiency causing dermatitis and alopecia. Deficiency of biotin in man has recently been produced by Sydenstricker and his colleagues. They found that after about a month their subjects got a fine scaly desquamation of the skin without pruritus; later there was a greyish pallor of the skin, atrophy of the lingual papillæ, mental depression and paræsthesiæ; anæmia was found and a large increase in serum cholesterol.

Conclusion

In the twelfth edition of this book vitamins were dismissed in a quarter of a page; at that time they were thought to have a narrow clinical application, being useful only in such classical diseases as rickets, scurvy, beriberi and pellagra. Through the rapid advance of biochemistry many vitamins have now been synthesized or isolated in highly concentrated form and in consequence a danger has arisen that diseases not of nutritional origin, such as diabetic neuritis, are diagnosed as deficiency diseases and treated with a pure vitamin to the exclusion of appropriate therapy. Further, it is improbable that a patient would be deficient in only one vitamin, even if he only had symptoms of scurvy or of beriberi. The consumption of an average mixed diet does not necessarily ensure protection because many factors (such as infancy and childhood, pregnancy and lactation) increase the requirement, and others (such as achlorhydria or diarrhœa) decrease the absorption from the gut or allow destruction. We still know little about dietary deficiencies in man, but we do know that slight deficiencies are quite common in this country; these facts should stimulate further clinical investigation and laboratory research. The relative ease with which several diseases in man can be treated with pure preparations of vitamins is unfortunately apt to overshadow the important problem of preventing nutritional disorders by ensuring that everyone consumes a well-balanced diet.

CHAPTER VII

THE ALIMENTARY TRACT

Diarrhœa

The Treatment of Diarrhœa.—The guiding principle in the treatment of all pathological conditions is that in order to obtain a cure it is necessary to determine the cause and to remove it. To seek only to alleviate symptoms brings to the patient a temporary relief from the inconvenience of the symptoms, but nothing more. There are, however, many causes of diarrhœa which may be very serious, as in cholera or dysentery, or trivial, as in acute diarrhœa without other symptoms. The usual directions for the treatment of acute diarrhœa are to give a dose of castor oil (1–2 drachms); this acts as a purgative and empties the large intestine and so removes the cause of the diarrhœa. To check the diarrhœa by the use of a preparation containing opium, which lessens the intestinal movement, is for most patients wrong, since the irritating or even toxic substances which are causing the diarrhœa may be absorbed and cause symptoms still more serious. The use of castor oil is, however, sometimes inconvenient, and another method of lessening diarrhœa is to give a powder which adsorbs the irritant substances. The best powder is kaolin, which is a finely divided china clay. It may be given in doses of 1–2 drachms suspended in water at intervals of half an hour. Other powders are charcoal and chalk, the latter being conveniently given as Mistura Cretæ B.P.C. Kaolin and chalk are both very suitable for children, while for adults bismuth salicylate, having the same adsorptive action, is given. All these substances are without chemical action on the surface of the intestine, though being fine powders they form a coating upon it.

Astringents.—Astringents are substances which have the property of forming a coating of coagulated protein on the surface of the intestinal mucous membrane and so reducing the sensitiveness of the mucous membrane to the action of substances in the alimentary canal. They are of two classes, the salts of heavy metals, and the vegetable astringents.

The salts of the heavy metals like ferric chloride or lead acetate precipitate protein. They are, however, little used internally. Pilulæ Plumbi cum Opio are pills combining the astringent action of lead acetate with the sedative action of opium. When a solution of lead acetate is mixed with a solution of albumin in a test-tube a precipitate of protein is formed; this precipitant action is the basis of the astringent property which lead acetate in common with other salts of heavy metals possesses. Mercuric chloride occupies a peculiar position among these salts, for the precipitate of protein first formed when it acts, redissolves in excess of mercuric chloride; hence when mercuric chloride comes in contact with the intestinal wall it corrodes the mucous membrane, and therefore gets its name of corrosive sublimate.

The best known vegetable astringents are kino, krameria, and catechu; all owe their astringent property to the tannic acid they contain. Kino is the dried juice obtained from the trunk of a tree growing in southern India; krameria is a dried root, and catechu is the dried aqueous extract from the leaves of a plant. Since tannic acid is the active constituent, it might be thought simpler to use tannic acid directly. For internal use this is inadvisable since it is irritating and may cause vomiting. When administered in the form of kino, krameria or catechu, the tannic acid is liberated slowly from a mixture with resinous substances, and the irritant effect is not observed. Vegetable astringents are used for treating inflammation of the colon, and are given together with chalk and tincture of opium as in Mistura Cretæ Composita B.P.C., the vegetable astringent in which is catechu, or else as powders combined with opium, such as Pulvis Kino Compositus, B.P.C., which contains 75 per cent. of kino and 5 per cent. of opium.

Opium in Diarrhœa.—One of the most important effects of opium and its active principles is that they produce constipation, and therefore can be used to lessen diarrhœa. Magnus investigated the action of morphine on the passage of a bismuth meal through the alimentary canal of the dog; he found that the shadow of the bismuth as seen by X-ray disappeared from the stomach of the normal dog in 3 hours and entered the colon at about the same time; after the administration of morphine hydrochloride in a dose of 6 mg.

per kg. the shadow disappeared from the stomach after 13 hours, and entered the colon not before this time. The delay is due principally to the spasm of pyloric sphincter and of the ileocolic sphincter, and also to the depression of the peristaltic activity of the intestinal wall. The different opium alkaloids vary in their action on the intestinal muscle. Papaverine has a strong depressant action and is known as an anti-spasmodic.

Some confusion exists about the action of morphine, the principal alkaloid of opium, on the alimentary tract. Some surgeons recommend morphine to increase peristalsis after an abdominal operation, and it is a well-known observation that morphine causes evacuation of the bowels when given to a dog. The explanation is that morphine has a stimulant action on the vagus centre in the medulla, which results in a discharge of impulses which slow the heart and also quickens the movements of the intestines. It is, however, wrong to use morphine for this purpose because its action on the intestines through the vagus nerve is readily overcome by its effect in closing the sphincter and producing constipation. The right drug to use is physostigmine (eserine) or else pituitary (posterior lobe) extract.

Babies and young children are much more susceptible to opium and its alkaloids than older people and these substances should be given to young children with great care.

Treatment of Diarrhœa in Cholera.—The treatment of diarrhœa in cholera is an excellent example of the danger of attempting to control a symptom. In cholera, or in bacillary dysentery, the diarrhœa is so severe that the patient may die from loss of water and loss of chloride; if, however, the diarrhœa is checked the patient may die from absorption of the toxins liberated by the bacteria. Rogers found that when opium was given the number of deaths was doubled. The two most important measures in treatment are to give kaolin in large doses to adsorb the toxins in the intestinal tract, and also to give hypertonic saline by intravenous injection. Rogers uses sodium chloride 1·3 per cent., sodium bicarbonate 0·6 per cent., and calcium chloride 0·05 per cent. The strength of sodium chloride, it should be noted, is about 50 per cent. greater than isotonic saline. A more concentrated solution cannot be given except in small volumes. The hypertonicity assists in retaining water in the blood vessels.

Small doses of potassium permanganate (0·1 gm. or 1·5 gr.) are given repeatedly by mouth to act as an intestinal disinfectant.

CONSTIPATION

The Causes of Constipation.—The large intestine has the duty of rendering unnecessary continuous evacuation of the fæces from the rectum. The contents of the small intestine pass into the large intestine as fluid containing solid matter suspended in it. The large intestine receives this fluid and absorbs the water from it; the solid matter is then evacuated once or twice a day. Constipation can occur:

(*a*) because too much water is absorbed and the fæces become too hard;

(*b*) because the fæces have too small bulk, and do not stimulate the intestinal wall to contract;

(*c*) because the intestinal muscle has temporarily lost its power of response to stretching.

Saline Purgatives.—The fluidity of the contents of the large intestine can be increased by the use of saline purgatives. The salts which are of use are those of which either the anion or the kation or both cannot be absorbed. Sodium sulphate can be used because the sulphate ion is not absorbed; magnesium chloride can be used because the magnesium ion is not absorbed; better, however, is magnesium sulphate, for neither of the ions is absorbed, but remain in the intestine and retain water there. That this effect is due to their osmotic pressure has recently been shown to be unlikely by the work of Lium and Florey, who consider that magnesium sulphate acts by arresting the absorption of sodium chloride from the intestine. Magnesium sulphate, or Epsom salts, is given as an isotonic solution before breakfast, that is to say as a 6·5 per cent. solution approximately; the dose of 8 gm. (or $\frac{1}{4}$ oz.) is dissolved in 120 c.c. water. When the stomach is empty the fluid immediately enters the duodenum and causes increased peristalsis. Magnesium sulphate should not be given in hypertonic solution because it causes closure of the pylorus.

Substances Increasing the Bulk of the Fæces.—Substances which increase the bulk of the fæces because they are not digested or absorbed in the passage down the alimentary canal are (*a*) cellulose, which is present in vegetables, fruits,

oatmeal, wholemeal or brown bread, (*b*) agar-agar and (*c*) liquid paraffin. Agar-agar and liquid paraffin are often combined in emulsions.

Irritant Purgatives.—These are substances which irritate the wall of either the small or the large intestine. Castor oil is obtained from the castor oil seed, and is the glyceride of ricinoleic acid; the oil itself has no effect in the stomach, but it is broken down in the small intestine, due to the action of lipase, and ricinoleic acid is set free; this exerts its irritant action at once, on the small intestine and also on the large intestine. Hence the action of castor oil is rapid, and it is usually given before breakfast, in a dose of 1–4 drachms. Castor oil is commonly believed to be harmless, but the colon remains flaccid and without its usual tone after castor oil has been taken.

The anthracene purgatives are cascara, aloes, rhubarb and senna; they are classed together because their active principles are derivatives of anthracene, two being emodin and chrysophanic acid. Emodin exists in the drug in combination as a glycoside. It is absorbed in this form through the wall of the small intestine into the blood stream where it is hydrolysed and then the active principle is excreted through the wall of the large intestine. It is during this excretion that the purgative action is exerted and this does not involve any extra activity on the part of the small intestine. The action of the drugs is slow because the stages of absorption and re-excretion take time; they are therefore given at night and cause evacuation in the morning. The active principle of aloes is aloin, and this when injected causes contraction of the uterus. Aloes is therefore not used in pregnancy. Rhubarb contains tannic acid, and the purgative action is often followed by constipation.

Phenolphthalein is now very widely used in advertised purgatives with proprietary names. It is cheap, and in ordinary doses without ill effect; it is partly absorbed in the small intestine and re-excreted by the liver in the bile; thus it enters the intestine for a second time, and exerts a further effect. If taken continuously it produces a toxic action on the kidney.

Calomel, or mercurous chloride is a powerful purgative, the maximum dose being 5 gr. (0·3 gm.) which is given at night and washed out by a saline purgative in the morning, since it is important not to allow the mercury to be absorbed.

It causes contraction of the intestinal wall of both small and large intestine. In small doses, such as $\frac{1}{10}$ gr., calomel is valuable for people who are liverish or bilious from over-feeding.

There are also the drastic purgatives, colocynth, jalap and croton oil. A well-known pill contains colocynth and hyoscyamus; the colocynth causes purgation, and the hyoscyamus, which contains atropine, by paralysing the parasympathetic nerve endings, prevents excessive and painful contractions of the gut wall. Croton oil is given in a dose of one drop on a piece of sugar or incorporated in butter.

Substances Given by Injection.—After abdominal operations there may be a partial paralysis of the intestinal movements, so that neither fæces nor flatus are passed. This is usually remedied by the injection of pituitary (posterior lobe) extract or by the injection of physostigmine, which increases the action of the parasympathetic nerves in bringing about intestinal movement.

The Use of Purgatives.—The right use of purgatives is difficult to indicate. Many people consider that in hospital wards purgatives are too widely used. For the treatment of sick people a hospital ward has serious disadvantages in that one patient disturbs another. In disease human beings do not sleep well under any circumstances, and when they are in a ward they sleep less well than in a single room. Hypnotics are therefore administered to make them sleep, and hypnotics have a constipating action, because they reduce the activity of the central nervous system, and in consequence the movements of the intestines. To remedy the constipation purgatives are given.

Before an abdominal operation it is also customary to purge the patient. Many believe that this does more harm by reducing the patient's strength than good by emptying the large intestine; it may also lead to post-operative ileus. If the large intestine is to be emptied, this is better accomplished by giving an enema than by purgation. When an enema is given the large intestine is distended with fluid and discharges its contents by a normal physiological response which does not dehydrate the body as a whole.

The choice of purgatives for different patients is important. It is not always realized that constipation in a breast-fed baby

is a very unimportant symptom, and that their bowels may remain unopened for several days without harm being done. For babies on an artificial diet the first choice is a purée of spinach or tomato with some increase of fluid intake. Liquor Magnesii Bicarbonatis B.P., or Fluid magnesia is the first drug which should be tried. For older children, cream of magnesia, of Mistura Magnesii Hydroxidi B.P. is given. If it is urgent to relieve constipation in a baby, grey powder, or Hydrargyrum cum creta B.P., consisting of 33 per cent. of metallic mercury with chalk, is given in a dose of 1–5 gr. The chalk enables the metallic mercury to be presented in a state of very fine sub-division.

In adults chronic constipation should be treated without the use of drugs if possible. Often extra fluid, as warm water before breakfast (up to 3 pints), fruit, especially apples, and exercise are sufficient to relieve this constipation. In some people preparations containing vitamin B_1, such as yeast extract (sold as Marmite) or wheat germ (sold as Bemax), are effective. When these steps are ineffective liquid paraffin should be tried. Of the substances which stimulate the large intestine, senna or cascara are probably the best. A cheap purgative is an infusion of senna pods made with cold water; four or five pods are allowed to soak in less than half a tumbler of water during the day, and the infusion is taken at bed-time. A more elegant preparation is Confection of Senna, but it is of course more expensive. Senna is a useful purgative for nursing mothers when it is important to choose a purge which will not be secreted in the milk and cause purgation in the baby.

Intestinal Fermentation.—If the fæces are unusually offensive, there may be unusual bacterial activity in the large intestine. This is lessened by giving adsorbent powders such as kaolin or charcoal. Activated charcoal, which has been treated with steam at high pressure, is more effective than ordinary charcoal. Similarly kaolin varies in fineness according to the care of preparation, and some manufacturers prepare a more effective powder than that which is official in B.P. 1932.

Intestinal putrefaction is also greatly benefited by the consumption of large amounts of sour milk. This is prepared by growing *B. acidophilus* or *B. bulgaricus* in pure culture in the milk. When these organisms are introduced in sufficient

quantity into the large intestine, other organisms diminish, and the putrefaction they cause is checked.

The Treatment of some Gastric Disorders

Hyperacidity.—There is great variation in the amount of hydrochloric acid secreted in the stomach of different individuals. In some the amount secreted causes the symptoms of gastric pain and heartburn, since relief from these symptoms follows the neutralization of the acid by substances which are classified as antacids. These are:

	gm.
magnesium oxide .	1
magnesium carbonate	2·3
sodium bicarbonate	4·0
calcium carbonate.	2·3
bismuth oxycarbonate	45·0

The weights placed against each substance are the relative amounts required to neutralize the same amount of hydrochloric acid. Thus the most efficient antacid is magnesium oxide and the least efficient is bismuth oxycarbonate. Magnesium oxide and magnesium carbonate both form magnesium chloride, which has a mild laxative action, and these are the best antacids when hyperacidity is accompanied by constipation. For this reason light magnesium carbonate is valuable to women in pregnancy, and can be taken daily in fairly large amounts; pregnant women often suffer from both hyperacidity and constipation. Calcium carbonate and bismuth oxycarbonate on the other hand both produce constipation to some extent, and can be given as antacids when the stools are too loose. It is insufficiently recognized that milk is perhaps the best antacid of all, and certainly the one the regular use of which produces no ill effects. Milk is the food provided for the newborn creature, and it is logical to suppose that in most diseases of the intestinal tract, benefit will follow the use of a milk diet.

Antacids are commonly prescribed mixed together, as in Pulvis Bismuthi Compositus B.P.C.; it contains bismuth carbonate 1 part, calcium carbonate 3 parts, heavy magnesium carbonate 3 parts, sodium bicarbonate 1 part. Such mixtures are known as MacLean's Powder and are taken by the general

public in very large quantities. Their continued use leads to excess of alkali in the body and sometimes to curious symptoms such as vaginitis, and soreness of the vulva. This may also occur in children who are regularly given magnesia as a laxative. Patients who complain of vaginitis should always be asked if they are taking alkalis.

Magnesium trisilicate is an antacid which does not make the body alkaline. It reacts with hydrochloric acid to form magnesium chloride and colloidal silica, which acts as an adsorbent.

Deficient Gastric Secretion.—Gastric secretion is caused by nervous stimuli passing along the vagi, and by chemical stimuli. The nervous stimuli travel as a reflex from the passage to the brain of impulses set up by the sight, smell and taste of food. The reflex is diminished by worry and anxiety. Alcohol, which diminishes worry and anxiety and the feeling of nervous exhaustion, therefore increases the secretion. Substances which act powerfully on the sense of taste also increase the secretion ; these are known as *bitters*, and include gentian, quassia and calumba. Quinine, nux vomica and its constituent strychnine also act in this way. Indeed it may be said that the chief use of strychnine in medicine is as a bitter tonic. The well-known preparation Easton's Syrup, or Syrup of Ferrous phosphate with quinine and strychnine, contains about 1 per cent. of quinine and 0·025 per cent. of strychnine. Bitters do not increase the flow of gastric juice when introduced directly into the stomach ; their action is exerted on the sensory nerve endings in the mouth.

The substances which act as chemical stimuli to the gastric secretion are first of all meat extracts and soups ; in contrast to the bitters these do not act in the mouth but in the stomach. Alcohol has also a direct stimulant action on the fundus causing the secretion of more gastric juice. Most of the substances widely advertised as tonics or restoratives in convalescence are either meat extracts, or contain alcohol or bitters. All these act by increasing the flow of gastric juice and so increasing the appetite.

Vomiting.—Vomiting generally arises from irritation of the gastric mucous membrane as a result of which impulses travel up the sensory fibres of the vagus to the brain, and efferent impulses pass down the phrenic nerves to the diaphragm.

Seasickness or airsickness is caused by impulses set up in the semicircular canals.

When it is desired to produce vomiting, emetics are used. Apomorphine is a central emetic, one, that is to say, which stimulates the medulla, and which is given by injection; morphine itself has an emetic action in a small porportion of people, and it frequently produces vomiting in dogs. As local emetics which act directly on the stomach, copper sulphate in 1 per cent. solution, or zinc sulphate in 1 per cent. solution, are used. Other substances which have a similar action when given in too large dose, though they are not used for this effect, are Ipecacuanha, ammonium carbonate or ammonium chloride.

CHAPTER VIII

ALCOHOL AND ANÆSTHETICS

Alcohol

Alcohol and the Central Nervous System.—The action of alcohol on the central nervous system used to be regarded as stimulant, but it is now considered depressant. In all persons except heavy drinkers, the consumption of alcohol reduces the efficiency with which work requiring mental concentration is performed. Quantitative studies have been made on compositors setting type and on persons doing typewriting, and these have shown that the number of mistakes in a given time is increased, though the effect of the same amount of alcohol varies in different people.

A further example of the same action is that after taking alcohol the driving of a motor-car is performed with less skill and judgment. In Sweden a chemical determination is made of the amount of alcohol present in the blood of drivers involved in accidents; this test has been criticized in this country on the ground that the amount of alcohol in the blood is no guide to the incompetence of the man, since some are unaffected by large amounts. The Swedish people are, however, satisfied with the test, for the amount of alcohol in the blood is a good guide to the amount which has been consumed, and they state that the variation in the extent to which different people are affected is exaggerated.

Since a substance which acts as a stimulant to the brain should increase the ease of concentration and of performing accurately work which demands skill, it is clear that alcohol is not a stimulant. How then is the apparently stimulating effect of alcohol to be explained as seen in the increase in talkativeness and in self-confidence which it produces? Normally the action of the highest centres of the brain produces impulses of modesty, self-criticism and shyness. Under the influence of alcohol, these impulses are depressed, and modesty and shyness diminish or disappear altogether; hence exuberance appears as a result of an inhibitory effect.

Alcohol and the Gastric Secretion.—In discussing the secretion of gastric juice, the action of alcohol in facilitating the psychic secretion has already been mentioned. The psychic secretion is caused by a nervous reflex arising in the organs for sight, smell and taste and passing from the brain along the vagus nerves. The reflex is depressed by anxiety and mental fatigue, and in consequence the appetite is less. Alcohol removes the feeling of anxiety and of fatigue and therefore increases the reflex and improves the appetite. For this reason alcohol is of benefit when taken before the evening meal, and it is suitably accompanied by bitters which themselves initiate the reflex.

Apart from this central effect, alcohol also acts directly on the gastric mucous membrane and stimulates a flow of gastric juice; observations on subjects with an œsophageal fistula have shown that if dilute alcohol is placed in the stomach beforehand, much more gastric juice is formed when meat is given by mouth but does not reach the stomach, coming out of the body through the fistula.

Concentrated solutions of alcohol have, however, a harmful effect on the stomach, for they inhibit the secretion. Those who consume a bottle of whisky a day have no free gastric hydrochloric acid.

Alcohol as a Food.—Alcohol is a food in the sense that it is completely oxidized in the body, and that the energy so produced is available for body needs. It is very rapidly absorbed from the stomach, though not more rapidly than cane sugar. Alcohol has therefore been used a great deal for patients in severe illnesses like pneumonia when the consumption and digestion of even a light diet is very difficult.

The use of alcohol in hospitals has now fallen to about 10 per cent. of what it was at the beginning of the century, and its importance is considered much less. If it is used, it should be given in small doses, often repeated, but it may be doubted whether it is better for sick patients than for athletes; since it reduces the efficiency of body mechanisms in health, it is probable that it adversely affects the body in disease.

Alcohol and the Circulation.—One of the best-known actions of alcohol is that it produces a feeling of warmth due to dilatation of the skin vessels. This effect causes increased heat loss, and alcohol must therefore not be given to those who are very cold before they have been put in warm surroundings. The dilator action on skin vessels is the basis of the antipyretic action of alcohol which is desired when those threatened with a cold take a hot whisky before going to bed.

That athletes in training must not take alcohol is now recognized; this may be because alcohol weakens the force of the heart beat, or impairs the musculature of the blood vessels or depresses muscle metabolism. That alcohol has an action on the peripheral vessels is evident from its action on the small blood vessels of the nose seen so clearly in chronic alcoholics. The effect on the efficiency of the body as a muscular machine varies greatly according to the subject; manual workers and those accustomed to an outdoor life are much less affected than sedentary workers.

Alcohol in Daily Life.—Alcohol in daily life is a useful hypnotic, and also useful in reviving appetite in fatigue; if, however, it is used for these purposes regularly, its hypnotic action disappears, and its effect on gastric secretion is offset by a reduction in general fitness. Alcohol, like all drugs, should be kept for occasional use.

Treatment of Intoxication.—In acute alcoholic intoxication the subject must be kept warm, and his stomach should be washed out to remove alcohol still unabsorbed. Death occurs from failure of the respiration, and oxygen containing 5 per cent. of carbon dioxide should be given to increase the respiration. In chronic intoxication the brain becomes accustomed to the presence of a certain concentration of alcohol, and if this is withdrawn symptoms such as delirium tremens follow. This is treated by hyoscine in doses of 1 mg. In

polyneuritis, when there is paralysis of the peripheral nerves, administration of the antineuritic vitamin is beneficial.

Methyl Alcohol.—The important difference between ordinary alcohol, which is ethyl alcohol, and methyl alcohol is that methyl alcohol is much more slowly oxidized in the body. Methylated spirit contains 10 per cent. of methyl alcohol, and wood spirit is mainly methyl alcohol. In man the toxic symptoms are coma lasting for some days, followed by bilateral inflammation of the optic nerve and retina. Frequently there is permanent blindness.

Anæsthetics

Chloroform and Ether.—When a patient is anæsthetized with either chloroform or ether the following stages succeed one another. Feelings of warmth, giddiness and suffocation; loss of consciousness and thereafter excitement; true surgical anæsthesia in which the muscles are relaxed; medullary paralysis affecting the respiration, but not the blood pressure. It is well known that chloroform weakens the heart muscle, but sometimes the statement is made that ether does not. Ether has, however, the same depressant effect as chloroform, though it is much less intense. In view of this action on the heart, the maintenance of the blood pressure in deep chloroform or ether anæsthesia is at first sight hard to understand. Both chloroform and ether cause a discharge of impulses along efferent sympathetic fibres, as was first shown by Elliott to be true of the splanchnic fibres running to the suprarenal gland. Similarly constrictor impulses pass to the walls of the blood vessels and raise the blood pressure. Because of the rise of blood pressure there is an increased coronary flow, and therefore in spite of the depressant action of the anæsthetic on the heart muscle, the heart's output of blood is maintained. Because of this action on the sympathetic system, both chloroform and ether inhibit the contractions of the uterus in labour.

Toxic Effects of Chloroform.—With chloroform there is a danger of sudden death during the induction. This danger is even greater for dogs than for men, but scarcely exists for cats. The cause of the sudden death is not known with certainty, but it may be due to irregularity of respiration

leading to a sudden intake of a high concentration of the anæsthetic, which causes heart failure by depressing the contractile power of the heart muscle. A second explanation is that there may be a secretion of adrenaline which causes the heart to fibrillate; it is in fact possible to cause fibrillation in the heart of a cat or dog by injecting adrenaline during chloroform anæsthesia; the adrenaline stimulates the cardiac muscle very violently and greatly increases the oxygen consumption to such a point that the heart is stopped for lack of oxygen. A third explanation is that death occurs because of excessive vagus slowing; it is certainly true that the chance of death is diminished by the previous administration of atropine, which paralyses the vagus nerve-endings.

A different form of injury which chloroform causes is delayed chloroform poisoning, which supervenes two or three days afterwards. This form of poisoning is produced not only by chloroform but by all halogen derivatives of methane, such as carbon tetrachloride. The symptom of delayed chloroform poisoning is vomiting, accompanied by ketonuria; if the patient dies, fatty degeneration of the liver and kidneys is found. Chloroform is now considered to be a dangerous anæsthetic, and in hospital work it is almost never used. If, however, a doctor has to give an anæsthetic in a private house in a room with an open fire, it is less likely to cause explosion than ether. Women in labour are said to be more resistant to the toxic action of chloroform than other patients.

Toxic Effects of Ether.—The depressant effect of ether on the heart is much less than that of chloroform. Ether, however, has the disadvantage that it is irritant to the trachea and bronchial mucous membrane, especially when no precautions are taken to warm the ether vapour. The irritant properties are greatly increased if the ether is exposed to light or air. It is sold in small brown bottles, and it should be used within 24 hours of opening the bottle, for increasing amounts of irritant peroxides are then formed. The irritation caused by ether leads to the secretion of much mucus, which may continue to block the finer bronchioles after the operation is over. Accordingly atropine is given before ether is used as an anæsthetic, since atropine dries up the bronchial secretion. It must not be supposed that the usual dose of atropine dries up all secretion, whatever the length of the operation, and it remains true that in spite of the use of atropine, bronchitis of

varying severity follows the use of ether in about 10 per cent. of patients.

The danger of this bronchitis can be greatly diminished by making the patient inhale oxygen containing 5 per cent. carbon dioxide; all the bronchioles are dilated, and the alveoli fully expanded. Stasis in the lower lobes is prevented. This inhalation is carried out two or three times after recovery from the anæsthetic, and again on the following days. Induction of anæsthesia with ether is alarming and unpleasant for the patient, and recovery from it is usually attended by vomiting. Patients feel particularly wretched. On the other hand it should be remembered that ether is the safest of all anæsthetics for major surgery because complete muscular relaxation is produced by concentrations of ether which are far less than those which cause arrest of respiration. Thus ether has a wide margin of safety in this respect, which is specially important when the person giving the anæsthetic has had little experience.

Shock Produced by Chloroform and Ether.—Both chloroform and ether produce changes in the circulation which persist for some days afterwards. Dale showed that normal cats can be injected with relatively large amounts of histamine without ill effect. If, however, histamine is injected during chloroform or ether anæsthesia, or during one or two days following the anæsthesia, then small doses produce a profound fall of blood pressure; the power of maintaining capillary tone against the dilator effect of histamine appears to be greatly diminished.

Nitrous Oxide.—Nitrous oxide is a gas which produces anæsthesia when given in high concentrations, and which is free from all the disadvantages of chloroform and ether. It has no action on the heart or the liver and it produces no irritation of the lungs. To produce narcosis, however, a concentration of 80 per cent. is necessary, and if the remaining 20 per cent. is air, then since only one-fifth of air is oxygen, the concentration of oxygen is 4 per cent., and the patient suffers from partial asphyxia. When nitrous oxide is used for extracting teeth, there is an obvious asphyxia, which can be maintained for very short periods only; accordingly the dentist must be quick. The asphyxia is attended by a rise of blood pressure which is dangerous for old people.

When nitrous oxide is mixed with oxygen, longer periods of anæsthesia are then possible. With 20 per cent. of oxygen, however, instead of 20 per cent. of air, the degree of anæsthesia is not so great, for the asphyxia caused by reducing the oxygen to 4 per cent. has some anæsthetic effect itself. Consequently 80 per cent. nitrous oxide and 20 per cent. oxygen is of value in dentistry only. A mixture of 89 per cent. of nitrous oxide and 11 per cent. of oxygen can be used for abdominal surgery, though muscular relaxation is difficult to obtain and there is some degree of asphyxia. Prolonged anæsthesia with asphyxia continuously present should be attempted only by experts. The alarming condition of the patient during the anæsthetic is, however, counter-balanced by the rapid recovery and absence of after-effects. Nitrous oxide is a valuable aid in child-birth, for it does not delay the progress of parturition.

Ethyl Chloride, being in chemical structure closely related to chloroform, has a similar anæsthetic action, but it is less toxic to the heart. It is a liquid which boils at 12·5° C., and therefore, when sprayed on to a surface, immediately evaporates and leaves the surface very cold. Ethyl chloride is unsuited for prolonged anæsthesia, and is chiefly used for children for short operations.

Ethylene is an anæsthetic which can be said to occupy a position midway between nitrous oxide and ether; it causes no irritation of the respiratory tract, and hence does not give rise to postanæsthetic bronchitis; it causes very little nausea and vomiting. When mixed with oxygen in the proportion of 90 per cent. ethylene and 10 per cent. oxygen, there is good muscular relaxation. The chief disadvantages of ethylene are that it forms an explosive mixture with oxygen, as ether does, and also that it has an unpleasant smell.

Cyclopropane, $(CH_2)_3$, is a gas which is heavier than air, with which it forms an explosive mixture. It is a very powerful anæsthetic since 4 per cent. produces some degree of narcosis; moreover it has no irritant action on the bronchial tract. It suffers from the disadvantage that there is no wide margin between the concentration which produces muscular relaxation and that which produces arrest of the respiration, so that sometimes when muscular relaxation is obtained, the patient stops breathing.

Divinyl Ether ($CH_2 = CH.O.CH = CH_2$) is very good for anæsthesia of less than 45 minutes duration. When administered for longer periods there is a danger of a toxic action on the liver. For dental work it is said to be excellent. Like ether it forms an explosive mixture with air, but it is less irritant and more powerful.

Basal Anæsthesia.—Non-volatile anæsthetics have the disadvantage compared with the anæsthetics considered hitherto that the concentration of anæsthetic cannot be rapidly varied at the will of the anæsthetist. The anæsthetic is given by intravenous injection, or per rectum, and if too large a dose is used the effect is irremediable. Since there is a wide variation in the amount of an anæsthetic required to produce the same degree of anæsthesia in different individuals, it follows that the dose sufficient to produce surgical anæsthesia in the majority of patients will produce in a small proportion so great a degree of anæsthesia that death will follow. In consequence of this the dose of a non-volatile anæsthetic should, if possible, be given very slowly, in order that the full effect of the amount already injected can be seen before more of the anæsthetic is given. If the dose cannot be given slowly, then the amount injected must be much less than that necessary to produce complete anæsthesia in the majority of patients, and can only be enough to produce a basal anæsthesia, which is then later increased to full anæsthesia by the use of a volatile anæsthetic like nitrous oxide or ether.

Morphine and Atropine.—It is scarcely correct to count as a means of producing basal anæsthesia the customary procedure of giving morphine and atropine before inducing anæsthesia with chloroform or ether. In ordinary doses morphine does not induce any great degree of anæsthesia, but it has the very important quality of diminishing the anxiety of the patient. Atropine paralyses the vagus nerve endings in the heart, and prevents excessive slowing ; also, by arresting the secretion of the glands in the bronchioles, it prevents the air way from becoming blocked with mucus.

Hexobarbitone and Pentothal.—Hexobarbitone used to be known as Evipan and is a cyclohexenyl derivative of barbituric acid. It is used as the sodium salt. This substance and pentothal are the two derivatives of barbituric acid which are used for producing full anæsthesia as distinct from

basal anæsthesia. Hexobarbitone is given intravenously in 10 per cent. solution, in amounts which may vary from 4–15 c.c., it is injected very slowly, a careful watch on the patient's respiration being kept. Hexobarbitone sends the patient to sleep at once without producing any excitement or distress, and produces complete anæsthesia; its action is very short and the patient quickly recovers. Pentothal is sodium ethyl- (l-methylbutyl)- thiobarbiturate; it is used like hexobarbitone but produces more complete relaxation and a longer anæsthesia. Both these substances owe their short action to the ease with which the sidechain is broken down in the body.

Pentobarbitone (Nembutal) and Amytal.—These substances are derivatives of barbituric acid which are not used for full anæsthesia but are used as basal anæsthetics, that is to say, to produce a certain degree of anæsthesia, not sufficient for a surgical operation but one which can easily be brought to completion by giving a small amount of ether or cyclopropane, or by giving nitrous oxide. These substances cannot be used for full anæsthesia because they are too dangerous, though their breakdown in the body is not slow.

Paraldehyde and Bromethol are substances which are given per rectum. Paraldehyde is used in a dose of 0·5 c.c. per kg. dissolved in water as a 10 per cent. solution; it is relatively feeble, but is used in children for tonsillectomy. Bromethol (Avertin) is tribrom-ethyl alcohol; it is supplied in solution in amylene hydrate in order to avoid the need of heat in preparing a solution. The solution contains 1 gm. per c.c., and the dose required is from 0·06 to 0·1 gm. per kg. for basal narcosis. Thus a patient weighing 50 kg. (or 110 lb.) requires 3–5 c.c. of the solution. Before administration it is diluted 30–40 times with water, and this dilution must not be acid to congo red, otherwise it is extremely irritant to the rectal mucous membrane. After absorption, which is rapid, the narcotic action is exerted and persists for two hours, followed by sleep for several hours. Avertin is combined in the liver with glycuronic acid to form urobromic acid. Toxic effects on the liver similar to those produced by chloroform have been described.

All substances used as basal anæsthetics depress the respiration to some extent, and after the operation is over there is a risk of stasis in the lower lobes of the lungs while the patient is inactive in bed. This risk can be minimized by

giving inhalations of oxygen containing 5 per cent. of carbon dioxide.

Spinal Anæsthetics. Spinal anæsthetics are usually given by lumbar puncture, though they have also been given through cisternal and dorsal punctures. The injection is made between the 3rd and 4th lumbar vertebræ in the mid-line. The effect of the anæsthetic when injected depends on the specific gravity of the solution in which it is dissolved. This can always be made greater than that of the cerebrospinal fluid by the addition of glucose. To inject a solution of smaller specific gravity than that of the cerebrospinal fluid, alcohol is added when necessary. If 0·5 c.c. of stovaine in saline solution of specific gravity 1·08 is injected into a patient who is sitting up, then if he remains in that position for a minute or two, the anæsthetic will sink to the bottom of the spinal canal, since the specific gravity of the cerebrospinal fluid is not more than 1·007; thus an area of low spinal anæsthesia is produced. If the patient is put on his back immediately after injection, the anæsthetic will sink to the dorsal region, because in this position the level of the spinal canal in the dorsal region is lower than that in the lumbar region; thus an area of abdominal anæsthesia is obtained. If after the injection the patient is placed flat on his face, the anæsthetic remains in the lumbar region.

Stovaine and procaine (novocain) have been much used for spinal anæsthesia, but the effect cannot be trusted to last more than one hour. A more prolonged anæsthesia is given by percaine, which is used as heavy percaine in a 0·5 per cent. solution containing 6 per cent. glucose, but chiefly as light percaine in a much weaker (1 in 1500) solution in distilled water.

In carrying out the anæsthesia, patients are given omnopon and hyoscine about 1½ hours beforehand, to lessen anxiety and induce forgetfulness. The induction of spinal anæsthesia causes a large fall of blood pressure, which assists the surgeon by diminishing bleeding, but is dangerous in heart disease. Usually the patient is safe so long as the facial or preauricular arteries are palpable; if not, 30 mg. (0·5 gr.) of ephedrine is injected intravenously.

Disadvantages are retention of urine, headache, ocular palsies and permanent paralyses. Retention of urine is treated with Carbachol B.P. (carbaminoylcholine, Doryl)

which, acting like acetylcholine, causes contraction of the bladder. Ocular palsies are very rare and always transient. Permanent paralysis is also rare. Headache is said not to occur in more than 1 out of 12 patients.

CHAPTER IX

CENTRAL DEPRESSANTS

The Physiology of Sleeplessness.—Certain areas in the thalamic region appear to play a part in controlling sleep, since, as Hess has shown, electrical stimulation of these areas in the cat enables sleep to be induced at will. This fact, though of great interest, does not help in the understanding of sleep so much as does a consideration of the activity of the parasympathetic system. The large snakes which swallow animals go to sleep during the process of digestion. Here is seen at once the relation between sleep and the taking of food. When an old man takes an after-dinner rest, he sits in a chair where he is warm and sleeps. His pupils constrict, his pulse rate becomes slow, his salivary glands are active, his bronchi constrict, his gastric, pancreatic and intestinal juices are freely secreted and his intestinal movements are unrestricted. Sleep is therefore related to increased activity of the parasympathetic system and to diminished activity of the sympathetic system.

Treatment of Sleeplessness.—In considering the treatment of sleeplessness therefore the first consideration is that patients should not go to bed when hungry; they should have a readily digested but satisfying evening meal. Wakefulness during the night is often removed by taking half a tumbler of water containing several lumps of sugar. A lack of fresh air and exercise is a common cause of sleeplessness; and physical fatigue, when not excessive, promotes sleep. Excessive mental activity is often allayed by reading in bed, and reading aloud is a soporific to the reader.

The use of drugs for sleeplessness is always to be avoided if possible. The most harmless hypnotic is sodium bromide, which can be given in a cup of meat extract; its action is, however, feeble on many patients, though not in all. Alcohol is useful as a hypnotic to those unaccustomed to it, especially if taken in quiet surroundings.

Hypnotic Drugs

The common hypnotic drugs are chloral, paraldehyde, sulphonal and the barbiturates.

Chloral Hydrate ($CCl_3CH(OH)_2$) is generally regarded as a safe hypnotic, though since its structure is not unlike that of chloroform, some believe it to be depressant to the heart, and therefore not to be used in patients with cardiac disorders. In the body it is reduced to an alcohol which combines with glycuronic acid and is excreted as urochloralic acid. Chloral hydrate is irritant to the stomach and to lessen the danger of vomiting is given well diluted together with syrup.

Paraldehyde $(CH_3CHO)_2$ is a safe anæsthetic with a very unpleasant taste. Although it is a liquid, it must be dissolved in water before administration ; a 10 per cent. solution can be prepared. Paraldehyde can be used to hide a more powerful hypnotic, which can be prescribed in a mixture two or three times and later omitted. The taste of the paraldehyde will then often suffice to produce sleep. Paraldehyde is excreted in the breath and for this reason is disliked as a hypnotic by those who have to nurse the patient.

Sulphonal has the formula :

$$\begin{matrix} CH_3 & & SO_2.C_2H_5 \\ & \rangle C \langle & \\ CH_3 & & SO_2.C_2H_5 \end{matrix}$$

it is used for producing prolonged sleep, and is of great value in psychiatric clinics. It is excreted unchanged, and at a very slow rate. The symptoms of overdose are cramp in the muscles, polyneuritis and skin rashes. Hæmatoporphyrin appears in the urine.

The Barbiturates.—Barbituric acid can be regarded as a compound of malonic acid and urea :

$$\begin{matrix} H & & COOH \\ & \rangle C \langle & \\ H & & COOH \end{matrix} + \begin{matrix} H_2N & \\ & \rangle CO \\ H_2N & \end{matrix} = \begin{matrix} H & & CO.NH & \\ & \rangle C \langle & & \rangle CO \\ H & & CO.NH & \end{matrix}$$

Barbitone itself is diethyl barbituric acid, in which the two hydrogen atoms of barbituric acid are replaced by C_2H_5 groups. Barbitone is often known by the proprietary name of Veronal, which is applied to the barbitone made by the German firm of Bayer. Barbitone itself is insoluble, and is administered in tablet form ; soluble barbitone is the sodium salt which is again often known by the proprietary name of

Medinal. Phenobarbitone is phenyl ethyl barbituric acid, and is often known by the proprietary name of Luminal. The barbiturates differ greatly in the duration and intensity of their action. These differences are due largely to the rate at which they are excreted. When barbitone is taken, at the end of 24 hours not more than 45 per cent. has been excreted, and even after 6 days, 20 per cent. still remains unexcreted. The excretion of phenobarbitone is very much slower, for after 24 hours not more than 3 per cent. has been excreted, and after 6 days only 15 per cent. If doses of barbitone are taken daily, the substance must accumulate in the body, and, during sleep, coma may ensue. The respiration becomes feeble, due to the effect on the respiratory centre, and broncho-pneumonia then commonly occurs. The treatment of barbiturate poisoning is to give the patient a mixture of oxygen and 5 per cent. carbon dioxide to breathe to make the respiration deeper and so expand the alveoli. The patient is stimulated by the intravenous injection of picrotoxin in doses of 10 mg. at intervals of one to two hours. As much as 160 mg. has been given in this way, with successful recovery of the patient. Picrotoxin has not been much used in medicine hitherto, as it has been believed to be a cerebral convulsant; this it is, but when used in barbiturate poisoning convulsions do not occur. In toxicity it is one quarter as powerful as strychnine and the ordinary therapeutic dose should therefore be about four times as great, that is to say from 8 to 32 mg. ($\frac{1}{8}$ to $\frac{1}{2}$ gr.). As there is little experience of its use in patients, doses of 10 mg. should probably not be exceeded at one time, though they may often be repeated. Picrotoxin is not very soluble, the maximum solubility being 0·3 per cent. so that the dose of 10 mg. is given in 3 c.c. It is far more effective in deep depression than is nikethamide (coramine) and much time is wasted in using the latter substance.

In summarizing the action of hypnotics, paraldehyde is the safest but most unpleasant. Carbromal, a pharmacopœial substance known as Adalin should be used much more than it is, since it is rapidly broken down. Barbitone and soluble barbitone are used much too freely, and many do not realize that Nepenthe owes its action to the opium alkaloids being similar in strength to Tinct. Opii. Sulphonal or phenobarbitone (Luminal) should be used for patients under constant observation only; their action is prolonged.

Opium

The most important alkaloids in opium and the average percentages of each are :

	per cent.
Morphine	10
Narcotine	6
Papaverine	1
Codeine	0·5
Thebaine	0·3

Morphine, codeine and thebaine are derivatives of phenanthrene, while papaverine and narcotine are derivatives of isoquinoline.

Properties of Morphine.—The action of morphine varies greatly in different species, and even in different animals of the same species. Thus in man a dose of 10 mg. ($\frac{1}{6}$ gr.) produces drowsiness, and it would be expected that a very much smaller amount would suffice in a frog ; this, however, is not so, for 10 mg. is also necessary in this animal. In the cat the usual action of morphine is to produce excitement, so that the cat rushes around the room ; in the dog morphine produces salivation, and often diarrhœa and vomiting ; narcosis then supervenes.

While in most men a dose of 10 mg. morphine produces an inclination to sleep, in some it produces nausea and in a few vomiting. Young children are extremely sensitive to morphine, and it should not be given to them except when absolutely necessary.

The best-known property of morphine is that it relieves chronic pain, and that it permits sleep when sleeplessness is due to pain. Not less important, however, is the power of morphine to relieve anxiety. When given to a patient before an operation the nervousness and apprehension are largely removed and the patient faces the operation calmly. It is this power of removing anxiety and depression which is the basis of the use of morphine as a drug of addiction. The two other important properties are the power to depress the cough centre, and the power to stop diarrhœa.

Morphine has very little effect on the higher centres of the brain, and the capacity for work remains for the most part unaffected. There is central stimulation leading to impulses passing down the third nerve to cause constriction of the pupil, and to impulses passing down the vagus causing slowing of the heart. There is depression of the respiratory centre so that the rate of respiration is slowed.

Morphine Poisoning and Addiction.—In poisoning there is narcosis accompanied by great respiratory depression; the pupils are constricted to pin-points. The treatment is to inject lobeline in order to stimulate the respiratory centre, and to give the patient oxygen with 5 or 7 per cent. carbon dioxide to breathe. The stomach should be washed out with potassium permanganate to destroy unabsorbed morphine; since morphine causes spasm of the pylorus, a good deal may remain in the stomach.

Repeated use of morphine always leads to tolerance, and may lead to addiction. The two conditions are entirely different, and should not be confused. Tolerance is the condition in which a given effect is produced only by a larger dose. Addiction is the condition in which the patient finds that he is distressed when the drug is withdrawn. When morphine is given, tolerance is shown after one or two weeks, so that to relieve pain more must be given. The patient then may form the habit of taking the drug and the cells of his tissues adapt themselves to the presence of a certain concentration of morphine. This is addiction. If morphine is then withdrawn cellular metabolism is deranged and the patient suffers from violent cramps in his muscles, and sometimes from collapse.

The morphine addict becomes degraded and completely untruthful. He shuns society, in this respect being unlike the heroin addict who seeks the society of other addicts. In treating addiction the early reduction of dose does not affect the patient so much as the final stoppage. The commonest method of effecting complete withdrawal of the drug is to keep the patient narcotized with hyoscine during 3 or 4 days.

Other Opium Alkaloids and Derivatives.—In the treatment of cough Tinctura Opii Camphorata, often called Paregoric Elixir, or Paregoric, has long been known to be of value. The alkaloids used for cough are heroin, which is diacetylmorphine, codeine, which is methylmorphine, and dionin, which is ethylmorphine. Heroin is extremely effective, but it produces addition very readily, so much so that in Egypt, in 1930, nearly 3 per cent. of the population were heroin addicts. Heroin should therefore be reserved for the intractable cough of pulmonary tuberculosis, or similar severe diseases. Codeine is a weaker alkaloid than morphine, having about one-twentieth of the narcotic action; on the cough and

respiratory centres it has, however, as much as one-third of the action and, like dionin, can be successfully used for cough with little fear of producing addiction. Codeine and dionin do not relieve pain.

After abdominal operations it is often desired to relieve pain without depressing intestinal movement; for this purpose heroin and also dilaudid, which is an oxidation product of morphine, are used; of the two dilaudid is the less dangerous.

Papaverine is often called an antispasmodic on account of its action on the intestinal muscle, the contractions of which are diminished. As sedatives in gastro-intestinal irritation the mixtures of opium alkaloids known as Omnopon and Pantopon are used.

Bromides

Use in Epilepsy.—Sodium and potassium bromide have a mild hypnotic action, as already described, but their chief use is in the treatment of epilepsy. Electrical stimulation applied to the motor cortex of the brain causes general convulsions throughout the body, but after the administration of bromides, convulsions are much less readily obtained. The beneficial effect of bromides in reducing the frequency of epileptiform attacks is attributed to this action on the motor cortex, by which the excitability of the cortex is reduced.

Bromides have to be given continuously in epilepsy and symptoms of overdose are readily seen. When the patient suffers from bromism, mental depression, skin eruptions beginning as yellow pustules, and muscular weakness are seen. Now bromides are excreted in the urine in parallel with chlorides; if much chloride is excreted, then much bromide is excreted; if little chloride is excreted, little bromide is excreted. When symptoms of bromism appear, they are most rapidly relieved by increasing the amount of sodium chloride in the diet, for the increased chloride intake results in an increased chloride excretion, and this is accompanied by an increased bromide excretion.

In order to obtain the maximum effect with a given dose of bromide, the chloride content of the diet should be reduced as much as possible. The normal intake of sodium chloride is about 10 gm. per day, and with care this can be reduced to 3 gm. Observations in epileptic colonies have shown that when great care is taken to exclude sodium chloride the average number of convulsions per patient is reduced to about 25 per cent.

Bromides of potassium, sodium and ammonium are used in medicine, but as the depressant action depends entirely on the bromide ion, they have all the same medicinal value. Organic bromine compounds have no depressant action.

Other Treatments of Epilepsy.—Phenobarbitone, better known as the proprietary form Luminal, is now much used in the treatment of epilepsy; the dose is small ($\frac{1}{2}$–2 gr.) (30–120 mg.) because it is excreted so slowly. Recently phemitone B.P. (Prominal) has been found more efficacious than phenobarbitone and in comparable series reduces the number of convulsions to 33 per cent. of the number under phenobarbitone treatment.

Epanutin, or sodium diphenyl hydantoinate, is a substance introduced as a result of experiments on cats, which is effective in epilepsy and is not a barbiturate. It can be tried in patients in whom barbiturate produce rashes or other undesirable effects.

The Atropine Group of Drugs

This group comprises:

1. Belladonna root.
2. Belladonna leaves.
3. Hyoscyamus leaves.
4. Stramonium leaves.

The alkaloids present in each are:

l-hyoscyamine
d-hyoscyamine
hyoscine (or scopolamine).

In the process of separating the alkaloids, the *l*-hyoscyamine and *d*-hyoscyamine come out together in the racemic form atropine. Hence the two alkaloids atropine and hyoscine are obtained.

Atropine and Hyoscine.—Atropine and hyoscine resemble one another in their peripheral action; both paralyse the action of the parasympathetic system and both dry up secretions. Atropine and hyoscine differ from one another in their central action, for while atropine is a central stimulant, hyoscine is a depressant. In general, atropine is used for its peripheral action and hyoscine is used for its central action.

Atropine.—The uses of atropine depend on its power of paralysing the action of the parasympathetic system. Thus

atropine is used to dilate the pupil in iritis and iridocyclitis when a prolonged dilation lasting two or three days is desired; the dilatation occurs because of paralysis of the third nerve, with relaxation of the circular muscle of the iris. The dilatation is accompanied by raised intra-ocular pressure since the resistance to the passage of aqueous humour through the canal of Schlemm is increased. When it is required to dilate the pupil for short periods only, for example to inspect the eye, atropine is not used, but rather homatropine, which is a synthetic substance having a much less persistent effect than atropine. When atropine dilates the pupil, the pupil will no longer react to light since the nerve-endings in the sphincter iridis are paralysed. Similarly under atropine the ciliary muscle is relaxed and in consequence the suspensory ligament is tightened; the lens, therefore, becomes flatter and only distant objects can be seen.

Atropine is used to prevent vagal slowing of the heart and salivation and the secretion of mucus by the bronchial glands during anæsthesia. Vagal slowing of the heart is specially prone to occur during chloroform anæsthesia, and the secretion of mucus is profuse during ether anæsthesia. Atropine dries up the bronchial glands as it dries up all other secreting glands, like the sweat glands and the gastric glands. Gastric secretion can be inhibited by the use of atropine in patients with gastric ulcer. Atropine has no effect on the blood vessels, and any effect it has on the blood pressure is due to increased heart rate after the removal of vagal inhibition. Babies suffering from broncho-pneumonia are often given atropine to stimulate the respiratory centre and to diminish the bronchial secretion; they become restless, very red in the face and extremely thirsty; nevertheless they tolerate atropine well.

Atropine Poisoning.—When an overdose of atropine is taken there is central excitement extending to delirium. The patient imagines that beautiful butterflies flutter before him.

Hyoscine.—Hyoscine is used as a depressant in delirium tremens and in the maniacal excitement of a lunatic. A dose of 1 mg. ($\frac{1}{60}$ grain) is usually given. Hyoscine is also used together with morphine in twilight sleep, because of its power of producing loss of memory. Small doses are given at intervals until it is found that the patient no longer remembers what she was talking about 5 minutes ago; this is the

condition of amnesia. Hyoscine is a constituent of some remedies for seasickness, exerting a central depressant action, so that the afferent impulses from the labyrinth fail to excite the vomiting centre in the medulla. Hyoscine is also used in Parkinson's disease to suppress the continuous muscular tremor by its central action.

Galenical Preparations.—Tincture of Belladonna is used on account of the atropine it contains to diminish pain due to violent contraction of smooth muscle in various organs. Thus it is used in cystitis to lessen the pain of micturition due to the contraction of the bladder; similarly it is used in dysmenorrhœa to lessen the pain of contractions of the uterus, though there is little evidence that the pain is reduced. Pilula Colocynthidis et Hyoscyami is a purgative pill in which the action of the drastic purgative colocynth is combined with hyoscymus to diminish the griping intestinal pains. Tincture of Stramonium is used in Parkinson's disease in the same way as is hyoscine; when given in large doses such as 3 c.c. or 75 minims, it has been found more effective than hyoscine.

CHAPTER X

THE DIGITALIS GLYCOSIDES AND HEART DISEASE

The Plants and Preparations.—There are many plants which contain glycosides having a digitalis-like action, but those principally used for the treatment of heart disease are digitalis and strophanthus. Outside this country squill is also much used. The best-known digitalis is *D. purpurea*, the purple foxglove, but a second important one is *D. lanata*; these contain the glycosides in the leaves and the seeds; the leaves are chiefly used. Similar glycosides occur in the seeds of strophanthus, of which *S. Kombé* and *S. gratus* are the most important.

Digitalis is used medicinally in the form (*a*) of the dried leaf compressed into tablets, (*b*) of the tincture which is prepared by extracting the dried leaf with 70 per cent. alcohol, (*c*) of infusion, which is prepared by extracting the dried leaf with hot water. Strophanthus is used in the form of tincture prepared from the seeds by first removing the fat, and then extracting them with 70 per cent. alcohol. Of these different

preparations Digitalis Pulverata, or Powdered Digitalis, the dried leaf compressed in tablets, is undoubtedly the best and should replace the others altogether. It is stable and can be given without danger of it being mixed with other things which may alter its potency; the stability of tincture and infusion is uncertain, and they may be mixed with other things. Infusion of digitalis is little used to-day, though some physicians like to give it because it was in this form that the drug was originally used by Withering in 1785. Powdered digitalis of course can only by given by mouth, but Tincture of Digitalis can also be given by rectum when patients persistently vomit. Tincture of Strophanthus is little used because it is said that its absorption is irregular. When tested on a frog or a cat Tincture of Strophanthus is about 45 times as potent as Tincture of Digitalis, and judging from this the dose of Tincture of Strophanthus ought to be one forty-fifth of the dose of Tincture of Digitalis. In fact the maximum pharmacopœial dose of Tincture of Strophanthus is as much as one third of the maximum pharmacopœial dose of Tincture of Digitalis; thus it is possible that the customary dosage of Tincture of Strophanthus is excessive, and its unpopularity is entirely due to this.

The Active Principles.—The most valuable active principle of digitalis is digoxin which is obtained from *D. lanata*. Digoxin is a pure chemical substance which can be given by mouth in a dose of 1–1·5 mg. or injected intravenously in a dose of 0·5–1·0 mg. Another active principle is digitoxin, but this when prepared by the usual process varies in composition and therefore in potency. It is the active constituent of the granules of Digitaline cristallisée of the French Codex, which, as prepared by Allen and Hanburys, are biologically standardized and do not vary in potency. These are given by mouth.

The glycosides of strophanthus are known as strophanthins. The strophanthin from *S. gratus* is a crystalline chemical substance known as ouabain. Large amounts of this substance have not been available hitherto, and therefore it has not had wide use. The strophanthin generally used is that obtained from *S. Kombé*, and, since it is amorphous, not always of the same potency; it should be biologically standardized as required by the British Pharmacopœia 1932; it is used exclusively for intravenous injection in a dose vary-

ing from 0·25–1·0 mg.; some workers consider that a dose of 1·0 mg. is too high, but others think that the lack of popularity which strophanthin has had is to be explained by the habit of giving too small doses.

Use of Digitalis in Disorders of Heart Rhythm

There has long been agreement that digitalis is of great value in the treatment of disorders of rhythm, especially in auricular fibrillation. The pathology of this condition is probably as follows. Attacks of tonsilitis lead to infection of the valves of the heart, especially the mitral valve, which becomes thickened. Incompetence of the mitral valve follows, with regurgitation of blood into the left auricle. This incompetence may grow worse until stenosis of the mitral valve occurs. A strain is then thrown on to the muscle of the auricle, which may hypertrophy. As a result of this strain, malnutrition of the auricular muscle arises and changes in conduction time accompanied by shortening of the refractory period occur. Auricular fibrillation then suddenly begins in which impulses pass around the auricle in what Lewis has called a circus movement, and the auricle, instead of contracting as a single muscle, contracts like a network of independently moving fibrils. The number of impulses passing from the auricles to the ventricles then increases from about 70 per minute to perhaps 400. The ventricle, attempting to beat as quickly as this, at once fails to pump efficiently, since between each contraction there is insufficient time for it to fill up with blood. Blood therefore accumulates on the venous side of the heart and heart failure occurs accompanied by cyanosis, dyspnœa, distress and œdema.

The patient can be treated by the oral administration of digitalis, but, given in this way, the patient gets relief very slowly. If doses of powdered leaf each 0·1 gm. or 1·5 gr. (equivalent to 1 c.c. or 15 minims of tincture), are given 4-hourly on the first day, to a total of 0·4 gm., and if on succeeding days he receives 0·4 gm., 0·3 gm., 0·2 gm. and 0·1 gm. respectively, the full effect is finally obtained in five days. Yet these are the usual full doses. Some authorities give the equivalent of 1 gm. of powdered leaf (or 10 c.c. or 150 minims tincture) on the first day, 0·5 gm. on the second, and 0·25 gm. on the third and fourth days, in order to obtain a more rapid action.

The very distressing symptoms of auricular fibrillation are most rapidly relieved by the intravenous injection of either strophanthin or digoxin, when the heart rate falls in 30–60 minutes.

The Action in Auricular Fibrillation.—The digitalis glycosides do not arrest the fibrillation in the auricles; it has been shown, however, that they diminish conduction in the bundle of His, which conducts the impulses from the auricles to the ventricles, so that the number of impulses which reach the ventricles falls from perhaps 400 to 100 per minute or less. The ventricles have therefore a longer time between each contraction in which to fill with blood. The main beneficial effect in auricular fibrillation which digitalis produces is due to the slowing of the rate of the ventricles. While the greater part of this slowing is due to the partial paralysis of the bundle of His, it is also due to increased vagal action, for if atropine is injected the ventricular rate rises. The increased vagal action is probably exerted on the vagus centre in the medulla. At least we know that digitalis exerts an effect on the medulla, for if digitalis is injected intravenously into a pigeon, vomiting follows in about 10 minutes.

Toxic Effects of Digitalis.—The obvious symptoms of digitalis overdose are nausea and vomiting, probably due to the action of digitalis on the vomiting centre in the medulla. A toxic effect is indicated by coupled ventricular beats or extra systoles which are seen in the electro-cardiogram. These are due to the increased irritability of the ventricular muscle as the amount of adsorbed glycosides increases past the optimal point. If the effect on the bundle of His proceeds too far, there is bradycardia, that is to say a very slow ventricular rate, and finally heart block.

Use of Digitalis in Patients with Normal Rhythm

While the use of digitalis for treating heart disease due to disorders of rhythm is generally recognized, it is not so generally recognized that digitalis is of value in treating weakness of cardiac muscle when there is no disturbance of rhythm. This is surprising since the ability of digitalis to increase the force of contraction of cardiac muscle is one of the best-known facts of pharmacology. Recently, however, the clinical observations of Fraenkel have emphasized the value of digitalis in treating œdema due to cardiac weakness, when the heart

rate is not raised, and even when it is very slow. Fraenkel has always used intravenous injections of strophanthin on the ground of safety since strophanthin is not a cumulative substance. When a single dose of digitalis is given the effect lasts for many days, and in treating patients with fibrillation, the maintenance dose required to keep the ventricular rate at an efficient level is much less than the dose given in the first few days to bring the heart under the influence of digitalis. If for any reason it is desirable to ensure that all digitalis

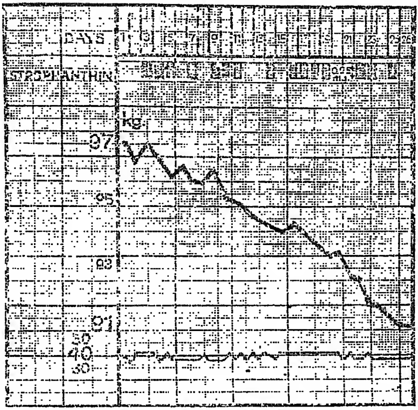


FIG. 9.—Showing the effect of injections of strophanthin on the body weight of a patient with cardiac œdema. The patient had arterio-sclerosis and a heart rate of about 40 per minute. Complete heart-block was present. (Fraenkel, 1935.)

effect has disappeared, it is necessary to wait from 2–3 weeks. With preparations of strophanthus, such as strophanthin, it is not necessary to wait, for the effect of a single dose has disappeared for the most part in 24 hours, and entirely in 48 hours; hence doses can be given every other day. Fig. 9 shows the effect of intravenous injections of strophanthin on the body weight of a patient with œdema due to cardiac weakness. The patient had arterio-sclerosis and a pulse frequency of about 40 per minute. The injections of strophanthin in doses of 0·25 mg. ($\frac{1}{240}$ gr.) were given almost daily. The

body weight fell from 97 to 91 kg. in 26 days, indicating a loss of 13 lb. of œdema fluid. This record is of course exceptional, for in this patient heart block was present throughout, and ordinarily the administration of a digitalis glycoside to a patient with heart block is contra-indicated; the record proves however that the efficiency of the heart can be increased by an action on heart muscle, and independently of an effect on heart rhythm. The digitalis glycosides can certainly be used when there is evidence of weakness of the heart muscle, as for example after illnesses, when there is congestion and œdema at the bases of the lungs.

The Action of Quinidine.—While digitalis restores the efficiency of the ventricle in auricular fibrillation, it does not affect the fibrillation itself. Quinidine, which is the dextro-rotatory isomer of quinine, does arrest the fibrillation and restore the normal auricular beat. Treatment with quinidine is preceded by rest in bed and a full course of digitalis. The first dose is 0·2 gm. (= 3 gr.) quinidine, given twice on the first day, and then, for four or five days, 0·4 gm. five times a day is given. If there is no restoration of the normal rhythm in this time, the treatment is discontinued. Restoration occurs in about half the early cases. The action is due to a lengthening of the refractory period of the auricular muscle, and the treatment is best applied to patients in whom the onset of fibrillation is recent. Quinidine also slows the rate of conduction, and this effect tends to neutralize the benefit of the lengthening of the refractory period. It is probably because of this that only a proportion of patients revert to normal rhythm. Sudden death has followed the use of quinidine in patients with long-standing fibrillation apparently due to the dislodging of a clot from the auricular appendix.

The Treatment of Angina Pectoris.—Angina pectoris is usually said to be due to insufficiency of the coronary blood supply to some part of the heart muscle, and is accompanied by intense precordial pain radiating down the left arm. The pain of an attack is relieved by agents which cause a fall in general blood pressure, which indicates that the insufficiency is only revealed when the blood pressure rises and the heart has more work to do. Angina cannot be treated by any routine treatment, but each attack must be dealt with either just before it comes on, or when it is in progress. In some

patients attacks are induced by muscular effort, and these can be prevented by putting tablets of glyceryl trinitrate (0·5 mg.) under the tongue when effort is about to be made. Absorption of the glyceryl trinitrate is more rapid under the tongue than it is when the tablet is swallowed. The action depends on the power of nitrites, such as amyl nitrite, sodium nitrite and of glyceryl nitrate (nitroglycerine) to relax the muscle of the arteries and so produce a fall of blood pressure. When the blood pressure falls the heart rate quickens as a result of less stimulation of the pressure receptors in the aortic arch and in the carotid sinus. Vagal tone is diminished.

When an attack is in progress, amyl nitrite, kept in small glass containers which are crushed in a handkerchief, is inhaled; this produces rapid relief accompanied by a sudden fall of blood pressure. The effect of amyl nitrite is however very short, while that of glyceryl nitrate lasts for one hour. When the pain of angina is not relieved by these agents, morphine must be injected.

Cardiac Asthma and Coronary Thrombosis.—Cardiac asthma is a medical emergency which arises in patients who have a high blood pressure. They wake up in the night gasping for breath, and are in acute distress. The condition is not due to constriction of the bronchioles, and can be relieved by morphine only.

In coronary thrombosis there is intense and long-lasting pain. This is not relieved by nitrites and can be relieved by morphine only.

CHAPTER XI

THE CONTROL OF THE CIRCULATION AND RESPIRATION

The Control of the Blood Pressure.—The blood pressure is controlled by a variety of factors of which three may be considered for present discussion; these are (1) the volume of circulating fluid, (2) the impulses passing along the vasomotor nerves, (3) the force of the heart beat. The first reason for which the blood pressure must be maintained is to

ensure a good coronary flow, for the coronary flow depends entirely on the blood pressure, and if this falls too low the heart stops. The second reason for which the blood pressure must be maintained is to ensure a blood supply to the brain, for if the respiratory centre is deprived of blood, respiration stops.

Loss of Blood.—The best means of raising the blood pressure after extensive hæmorrhage is to give a blood transfusion. It is commonly believed that for this purpose, blood after being collected from a donor may be kept for three weeks, and used at any time within this period. A varying percentage of blood becomes contaminated when it is drawn, and some think that whole blood should be used only when fresh. When fresh blood is not immediately available serum can be used. Since serum is passed through a bacteria-proof filter before it is finally bottled it is sterile. Serum is stored as liquid serum or as dried serum which is re-dissolved by addition of distilled water. When the drying is carried out in a vacuum at low temperature, the proteins are not altered in constitution. When serum is given initially, fresh blood can be given the following day to replace the lost corpuscles. Sterile plasma is also used instead of serum.

Treatment of Shock due to Burns.—Serum or plasma is also valuable in the treatment of the shock which sets in a few hours after extensive burns; it is accompanied by a fall in blood pressure and a reduction in blood volume indicated by an increase in the hæmoglobin percentage; there is also a rise in body temperature; the injection of serum restores the blood pressure and brings down the temperature.

Medullary Stimulants.—In the medulla is a vasomotor centre from which the impulses originate which leave the spinal cord in the sympathetic pathway and proceed to the blood vessels. The vasomotor centre receives afferent impulses from various points, notably the carotid sinus; if the pressure in the carotid sinus falls, as for example when clips are placed on the carotid arteries in the neck, afferent impulses pass from the sinus to the centre and in response more impulses leave the vasomotor centre causing increased vasoconstriction and a rise in blood pressure. In theory therefore it should be possible to raise the blood pressure by stimulating the vasomotor centre by medullary stimulants, which either stimulate the centre directly or make it more

sensitive to the afferent impulses it receives. In patients dying from pneumonia it has often been the custom to inject strychnine every four hours; this causes increased vasoconstrictor impulses, increased coronary flow and improved heart beat. Strychnine has no direct action on the heart, but it benefits the heart by this indirect method.

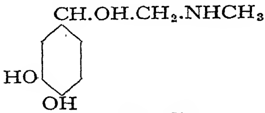
There are three other substances having a similar effect to that of strychnine. These are picrotoxin, leptazol (cardiazol) and nikethamide (coramine). Leptazol is pentamethylene tetrazol and nikethamide is the di-ethylamide of nicotine acid. According to animal experiments there is very little difference between strychnine, picrotoxin, leptazol and nikethamide, so far as their effect on the vasomotor centre is concerned. In decerebrate cats, the carotid sinus reflex (the rise of blood pressure obtained by clamping both carotid arteries for one minute) can be depressed by the injection of a barbiturate such as nembutal and the depressed reflex can then be restored by the injection of any of the four substances. The doses necessary in the cat however are a very large fraction of the doses which are ordinarily injected in therapeutics, and it is clear that if 40 or 50 per cent. of the human dose is required to stimulate the vasomotor centre of a cat, a therapeutic dose can have little effect on the vasomotor centre of man.

The value of these medullary stimulants to restore a failing circulation is therefore very small, and indeed it does not often happen that the circulation fails because of an insufficient stream of impulses from the centre. The failure is more often due either to a progressive weakening of the heart muscle, or else to a failure of the sympathetic impulses to cause vasoconstriction, as appears to happen in secondary shock due to burns, or in wound shock. This failure of sympathetic impulses to cause vasoconstriction may be due to deficiency of the cortical hormone.

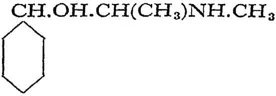
Sympathomimetic Agents.—When it is desirable to raise the blood pressure the most efficient substances are those which act directly on the heart and blood vessels increasing the force or rate of the former and constricting the latter. Adrenaline itself cannot be employed for this purpose since its action is too violent and too transient. There are, however, several other substances with an adrenaline-like action which to a greater or less extent imitate the action of the sympathetic system. The best known of these are ephedrine, ~~pholedrine~~

(Veritol), neosynephrine (meta-Sympatol, not to be confused with para-Sympatol which is much less active) and amphetamine (better known as Benzedrine), though this is used for a different purpose.

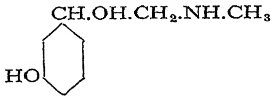
Ephedrine differs from adrenaline chemically as shown in the following formulæ :



Adrenaline



Ephedrine



Neo-synephrine

Ephedrine differs from adrenaline in that it has no -OH groups in the benzene ring, and that it has a $-CH_3$ group attached to the α carbon atom. These chemical differences make it much more stable than adrenaline ; in particular the $-CH_3$ group on the α carbon atom prevents its destruction by the amine oxidase which is believed to be the principal enzyme which destroys adrenaline at least in the liver. Ephedrine attaches itself to sympathetic receptors and in doing so produces sympathetic effects. Since it is removed only by diffusion and not by enzyme action, the duration of its action is long. Although ephedrine is not destroyed by amine oxidase, it inhibits the action of the enzyme in destroying adrenaline ; probably it does this by becoming attached to a proportion of the molecules of enzyme, so that there are fewer molecules of enzyme free to destroy adrenaline. Thus ephedrine has two actions ; an action of its own which is prolonged, and an action whereby the effect of adrenaline (or sympathetic nerve impulses) is intensified.

Ephedrine is chiefly known as a remedy for asthma which exerts its effect when taken by mouth. After absorption it causes dilatation of the bronchioles. Ephedrine is also used in solution as a nasal spray for its vasoconstrictor effect on the mucous membrane of the nose in hay fever. It has a similar

action on the heart and blood vessels to that of adrenaline. The chief action is on the heart muscle whereby the rate and force of the beat are increased; the constrictor action on the blood vessels is relatively small. Ephedrine is used to restore the circulation if during spinal anæsthesia the anæsthetic paralyses the roots which carry sympathetic impulses to the splanchnic area; a large fall of blood pressure then occurs which is detected by the disappearance of the pulse in the temporal arteries. An intramuscular (or intravenous) injection of 30 mg. ($\frac{1}{2}$ gr.) ephedrine hydrochloride is then given.

For the treatment of circulatory failure in pneumonia, neosynephrine has been successfully used, for it can be given repeatedly, at hourly intervals, with undiminished effect. If ephedrine is given repeatedly its effect declines and is very small when the third and fourth dose is given. Thus neosynephrine is distinctly superior to ephedrine for repeated injection. On the other hand the duration of the action of neosynephrine is short. Pholedrine (Veritol) has an action more prolonged than neosynephrine and similar to that of ephedrine in duration; repeated injections of pholedrine produce effects which do not greatly decline. Neosynephrine does not increase the heart rate of the isolated heart though it increases the force of the beat and its effect in raising the blood pressure is largely due to vasoconstriction. Both ephedrine and pholedrine have less action on the blood vessels and relatively more on the heart, though there is evidence that pholedrine causes the blood in the liver and spleen to pass into the general circulation.

Amphetamine (Benzedrine).—This substance, which is β-phenylisopropylamine, is volatile and is absorbed when inhaled. It was first introduced to diminish nasal congestion by its vasoconstrictor action on the mucous membrane of the nose, and it was then found to have an action on the central nervous system. When injected intravenously in animals it produces an augmentation of the action of the heart and a rise in blood pressure similar to that produced by ephedrine. The most striking feature of its action in man is that in many people it increases the power of mental concentration and the capacity to concentrate for long periods without fatigue. If taken in the afternoon, benzedrine interferes with sleep. The effect on the central nervous system varies in different people, and in some unpleasant symptoms of nausea and dizziness occur.

Adrenaline is used in medicine in the treatment of asthma; the subcutaneous injection of 0·2 c.c. usually produces prompt relief by causing dilatation of the smooth muscle of the bronchioles. Adrenaline is also used in local anæsthesia, especially with procaine (novocaine) to prolong the duration of the anæsthesia. When adrenaline is not used, the procaine is rapidly carried away by the blood from the site of injection. Adrenaline is also used when untoward effects follow the injection of serum, such as diphtheria antitoxin. In some patients anaphylaxis occurs, and the prompt intravenous injection of adrenaline can alone save them. In serum rash, or urticaria resulting from food poisoning or from sensitiveness to certain drugs such as aspirin, adrenaline causes disappearance of the rash and of the symptoms.

Respiratory Stimulants.—The best stimulant of the respiratory centre is carbon dioxide which is given as 5 or 7 per cent. of a mixture with oxygen. It is of great value in resuscitation after drowning, and carbon monoxide poisoning, and in starting breathing in the newborn. In the treatment of morphine and barbiturate poisoning the mixture has the additional advantage of dilating the bronchioles, and also in lessening the risk of bronchitis in those who have had an anæsthetic by the same action which opens the bronchial airways.

Of substances which depress the respiration the most important are morphine and allied substances and derivatives of barbituric acid. Substances which stimulate the respiration include lobeline, caffeine, picrotoxin, leptazol, nikethamide and atropine. Probably lobeline is the best, and it is difficult to place the others in order of merit. Their effect is transitory when the respiration has once stopped, and is often restricted to the production of gasping. Often the respiration improves when the blood pressure is raised, presumably because of the improved blood supply to the centre, and the injection of pholedrine (veritol) and ephedrine may therefore result in increased rate and depth of respiration.

The Administration of Oxygen.—In health the arterial blood is 95 per cent. saturated with oxygen, but in pneumonia the degree of saturation is less, depending on the severity of the disease; it may not be more than 68 per cent. saturated, and the oxygen tension corresponding to this low degree of

saturation is only 38 mm., instead of 100 mm. In this condition the tissues are suffering from oxygen deprivation, and it is therefore essential to administer oxygen. In considering the amount of oxygen to be given, it should be remembered that a patient in fever probably breathes 10 litres of air a minute, of which one-fifth, or 2 litres, is oxygen. This amount of oxygen must at least be doubled, that is to say not less than 2 litres of oxygen per minute must be supplied. If oxygen bubbles through water as fast as can be counted, the volume is about one-tenth of this, or 0·2 litre per minute. The oxygen must be pushed until the patient loses all trace of cyanosis.

Oxygen is now usually given by a face mask connected to a bag to collect the oxygen delivered to the patient during expiration, so that this oxygen is not wasted. The patient breathes out of the bag, and expires through a valve. The bag must be large enough not to be emptied by the deepest inspiration, and the valve must oppose no resistance to expiration. Usually some device permits the oxygen coming from the cylinder to be diluted to any desired extent with air, so that sufficient oxygen is given to keep the patient's colour pink, but not more than enough to do this.

The Treatment of Cough.—For the treatment of cough the morphine group of alkaloids are the most important. Heroin, or diacetylmorphine, is the most potent, but its use so often leads to addiction that it should be reserved for incurable patients suffering from the late stages of phthisis or from carcinoma of the lungs. Morphine relieves cough, but because of the danger of addiction it should not be used if codeine is a satisfactory substitute as it nearly always is. Codeine is not so powerful a depressant of the cough centre as morphine, having only one-third the potency. But codeine has almost no narcotic effect, at most 5 per cent. of that of morphine, and therefore does not lead to addiction.

In children opium alkaloids, even codeine, must be used with care as the respiratory centre is more easily depressed. Cough in children is commonly treated with Ipecacuanha, in the form of tincture, which acts as an expectorant, producing increased bronchial secretion by reflexes initiated by stimulation of the sensory nerve endings of the vagus in the wall of the stomach, and passing from the vagus centre to the bronchial glands.

The Treatment of Chronic Bronchitis.—The most important step in the treatment of chronic bronchitis is the administration of cod-liver oil. With the recent growth in knowledge of the action of vitamins, earlier observations have been forgotten, and especially the protective and curative action of cod-liver oil in pulmonary diseases. Whether this action is due to the vitamins present in cod-liver oil is unknown, and therefore it is important that other fish oils, such as halibut oil, or vitamin concentrates, should not be used instead of cod-liver oil. Patients with chronic bronchitis should be sent to live in a dry atmosphere if they can afford this.

CHAPTER XII

THE ACTION OF DRUGS ON THE UTERUS

Pituitary (posterior lobe) Extract.—The action of pituitary extract on the uterus was described by Dale in 1909, and since that time the history of its use in midwifery has been interesting. In the period up to 1925 there was no standard for the potency of different preparations ; some were inactive and some were much stronger than it is now considered right that they should be. Some manufacturers failed to realize the danger of too active preparations, and similarly many doctors preferred preparations which produced a rapid effect without doing immediate and obvious harm.

During labour the contractions of the uterus are first concerned in dilating the os uteri to such a point that the head of the child can pass through it ; this is the first stage. In the second stage the child is pushed out of the uterus, through the vagina, and is born. In the third stage the placenta is expelled. These changes must take place gradually if there is to be the minimum of damage to the maternal passages, and if they are not to be torn. A large dose of pituitary extract produces a powerful contraction of the uterus maintained for 10 minutes, and followed by intense activity of the uterine muscle, in which contraction and relaxation alternate. The expulsive force on the child is great. In consequence,

while pituitary extract in the early days of its use was found to accelerate the course of labour, greatly to the convenience of the doctor, it was also found to be dangerous, for in some patients rupture of the uterus was recorded. As a result prudent obstetricians abandoned its use in the first and second stage of labour, and used it solely in the third stage of labour to arrest post-partum hæmorrhage. This remains to-day the chief application of pituitary extract in midwifery.

After 1925, however, an international standard was introduced as a result of which preparations were uniform in activity. An international unit was described and the extracts were all prepared to contain 10 units per c.c. Investigation of the action of different doses in the first and second stages of labour showed that there was great variation in response to the same dose; 2 units, corresponding to 0·2 c.c. of ordinary extract, produced an effect as great as would ever be desired in some patients and a transient, very slight effect in others. The conclusion was drawn that before delivery of the child the dose used should never be more than 2 units, and that this should be given only when the os was approaching full dilatation.

Oxytocin and Vasopressin.—Pituitary extract has been separated into two fractions, oxytocin (sold as Pitocin) and vasopression (sold as Pitressin). The action on the uterus is exerted by oxytocin only. The advantage of its use is that untoward symptoms have been recorded after the injection of 10 units (1 c.c.) of pituitary extract for post-partum hæmorrhage. Collapse, lasting for about 20 minutes, has been seen, and this appears to be due to the effect of the vasopressin fraction of the extract. The reason for the action is unknown, but it may be that in some occasional patients a large dose of pituitary extract causes sufficient constriction of the coronary arteries to cause collapse. No fatalities have occurred from this cause. It is to be remembered that pituitary extract like adrenaline causes vasoconstriction of the arteries; while however adrenaline dilates the coronary arteries, pituitary extract constricts them.

The Action of Ergot.—The action of ergot on the uterus has been known for several hundred years at least. The first physiologically active alkaloid to be isolated from it was

ergotoxine, which was detected by its power to reverse the action of adrenaline on the blood pressure. After the intravenous injection of ergotoxine into a cat, the injection of adrenaline causes a fall of blood pressure instead of a rise. Some samples of ergot contain an alkaloid ergotamine which differs chemically from ergotoxine, but which has the same physiological properties. Ergotamine, moreover, is sold under the proprietary name Femergen, so that there are at least three names corresponding to one physiological effect. Until a few years ago, ergotoxine or ergotamine was believed to be the specific alkaloid which was responsible for the traditional action of the drug. It is now known that this is not so, and that ergometrine is the clinically important principle. Ergometrine is also described by many other names, such as ergobasin, ergostetrin, etc.

Ergometrine is a substance which when given by mouth exerts an action on the uterus in 4 or 5 minutes ; in this respect ergometrine differs completely from ergotoxine, for although ergotoxine is absorbed from the stomach the rate of absorption is very slow. The effect of ergometrine on the uterus is to produce a rise of intra-uterine pressure which is at first maintained, and then gives way to alternate contraction and relaxation; it is not an effect which it is desirable to produce while the child is in the uterus, but it is most efficient in arresting post-partum hæmorrhage. Ergometrine has little if any action on other tissues of the body.

Ergotoxine also causes a contraction of the uterus when injected subcutaneously, the effect coming on after about 20 minutes. The contraction resembles a spasm of the musculature which is maintained for long periods. In addition to this effect on the uterus, ergotoxine (and of course ergotamine also) causes constriction of the capillaries throughout the body. Thus in a cockerel the capillary constriction leads to gangrene of the comb, and continued administration in patients (which has occurred accidentally because the drug was not stopped by the doctor) leads to gangrene of the fingers or toes. The form of ergotism known as St. Anthony's fire depicted in old illuminated MSS. and stained-glass windows, in which hands and legs dropped off, was due to the ergotoxine (or ergotamine) absorbed in eating bread made from rye infected with ergot. Ergotamine is today recommended for use in the treatment of migraine, but its action is not understood.

Ergot Preparations.—Ergot is used in medicine today in two forms, prepared ergot and liquid extract of ergot. Prepared ergot consists of powdered ergot from which much of the fat has been removed, and which is adjusted to a fixed percentage of ergotoxine. Since ergotoxine is an undesirable ingredient, prepared ergot should not be used. The liquid extract of ergot of B.P. 1932 is obtained by percolating the powdered ergot with acid alcohol; thus the extract contains both the ergometrine and the ergotoxine. Ergotoxine in solution is however very unstable, and by the time it is used the liquid extract contains only small amounts. The extract also contains histamine, but not in sufficient quantity to exert an action on the uterus. The injection of 2 mg. histamine under the skin produces a striking effect on the parturient uterus, which lasts for half an hour; so large a dose as this cannot ordinarily be given, because of the bronchoconstrictor action of histamine.

The Action of Adrenaline and Anæsthetics.—An intravenous injection of adrenaline causes a temporary inhibition of the contractions of the uterus in labour, as also does anæsthesia induced by either chloroform or ether. Anæsthesia with nitrous oxide does not interfere with uterine contractions.

Other Properties of Pituitary (posterior lobe) Extract.—It is convenient at this point to discuss the other properties of pituitary (posterior lobe) extract. The name pituitrin is often used for this extract, but this is the proprietary name of Messrs. Parke, Davis and Co. The first property which was discovered was the pressor property. Pituitary extract is scarcely ever used for this purpose, since a rise of blood pressure is obtained only after intravenous injection. After subcutaneous injection a greenish pallor of the skin is seen, but the blood pressure does not rise. The pressor effect is exerted on the muscle of the blood vessel walls, and persists after paralysis of the sympathetic nerve endings.

Pituitary extract has an antidiuretic action which is used in the treatment of diabetes insipidus, a disease in which patients pass excessive amounts of urine, and drink corresponding amounts of water. The disease is due to the failure of the kidney tubules to reabsorb water. The antidiuretic effect of pituitary extract can be demonstrated in normal individuals by injecting the extract at the same time that one pint of water

is drunk. The excretion of the water is then delayed for several hours. The antidiuretic action is exerted by the vasopressin fraction of pituitary extract, and not by the oxytocin fraction.

Pituitary extract is used in the treatment of post-operative ileus, which is a condition after an abdominal operation in which the patient cannot pass fæces or flatus. The injection of the extract increases the peristaltic movements of the intestines, though, curiously enough, pituitary extract has little or no action on strips of isolated intestine suspended in Ringer's solution.

In the treatment of retention of urine after childbirth, when the bladder fails to contract, pituitary extract is not used. Instead, Doryl, which is carbaminoyl choline, is used with good effect. This can also be used in post-operative ileus.

CHAPTER XIII

CALCIUM, IODINE, THE PARATHYROID AND THYROID GLANDS

The Need for Calcium in the Diet.—In order to have strong bones, a child requires 0·9 gm. of calcium daily. Since milk contains about 0·1 per cent. of calcium (an amount similar to the amount of sugar in the blood), a child requires one and a half pints of milk a day. Besides milk the only other important source of calcium in food is cheese. The attention which has recently been paid to the importance of vitamin D in bone formation has partly obscured the need for calcium. This need is however well illustrated by recent experiments of Coward, Kassner and Waller (1938) in which they fed groups of rats on a diet approximating in composition to that of poor people. The diet was carefully prepared so that it was identical for different groups of rats. One group of rats acted as controls, a second group received cod-liver oil in addition to the diet, a third group received halibut-liver oil and a small amount of milk, while a fourth group received Virol. In Table VII are shown the mean growth of the different groups, and also the mean percentage of ash in the bones.

TABLE VII

GROUP.	SUPPLEMENT TO DIET.	MEAN INCREASE IN BODY WEIGHT IN 6 WEEKS.	MEAN PERCENTAGE OF ASH IN BONES.
		gm.	
1	None	43	40
2	Cod-liver oil . . .	68	38
3	Halibut oil and milk	79	39
4	Virol	46	39

The significant result of the experiment is that in all four groups of rats the percentage of ash in the bones, representing the amount of calcium in the bones, was very low, and that the addition of cod-liver oil or of halibut oil to the diet, although it increased the body weight, did not increase the amount of calcium deposited in the bones. In a second experiment all the rats were given the diet together with cod-liver oil, but a salt mixture was added in varying amounts for different groups, as shown in Table VIII.

TABLE VIII

GROUP.	AMOUNT OF SALT MIXTURE OR MILK ADDED.	PERCENTAGE OF ASH IN BONES.	MEAN INCREASE IN BODY WEIGHT.
1	None	40	50
2	0·02 gm. S.M. . .	43	54
3	0·06 gm. S.M. . .	48	54
4	0·18 gm. S.M. . .	52	57
5	5 c.c. milk . . .	46	78
6	Milk *ad lib.* . . .	52	105

In groups 5 and 6, salt mixture was not added to the diet, but milk instead. The results show that the percentage of ash in the bones rose in groups 2, 3 and 4 according to the amount of salt mixture in the diet up to the figure of 52 per cent., which is about the maximum. The addition of 5 c.c.

of milk per rat did not produce maximal deposition of calcium, but milk *ad libitum* did. The results are a striking indication of the necessity of relatively large amounts of calcium for the growing child, in addition to supplies of vitamin D. 5 c.c. of milk per rat of 80 gm. is equivalent to $1\frac{1}{2}$ litres of milk for a child of 56 lb., which is an indication for calcium requirement in children similar to that already stated.

Absorption of Calcium.—The absorption of calcium is well-known to depend on the amount of vitamin D in the diet, but it depends also on the proportion of phosphate in the diet. In the rat absence of vitamin D does not produce rickets unless the phosphate is reduced until the ratio of calcium to phosphorus is 2 : 1 or even 4 : 1.

In cereals such as oatmeal or wheat, phosphorus is present in the form of phytic acid, which is inositolhexaphosphoric acid. This substance combines with calcium in the diet and forms an insoluble salt which is not absorbed. Mellanby first showed that when young dogs were fed on the same diet with the difference that the one was given oatmeal and the other white flour, the dog eating oatmeal developed the worse rickets. White flour, although made from another cereal, wheat, contains very little phytic acid because this is removed, together with bran and the germ. Brown flour, however, contains more phytic acid, and on a diet poor in milk and cheese and therefore poor in calcium, brown flour leads to the same deficient calcium absorption as does oatmeal. Brown bread, when this constitutes an important part of the diet, and when the diet includes little milk or cheese, should be fortified by the addition of calcium carbonate.

Action of Calcium in the Body.—The action of calcium on the circulation is not well understood, but calcium can be considered to act in some respects like adrenaline, and it is for this reason that the intravenous injection of calcium may have some justification. Calcium appears to diminish the permeability of the capillary vessels, and so to prevent exudation of fluid outside them. Thus may be explained the beneficial action of calcium in chilblains and in urticaria; similarly calcium is beneficial after the injection of serum to lessen the incidence of serum rashes. The relation between calcium and adrenaline is well seen in the isolated heart of the frog, in which the effect of adrenaline is often slight. If

however the heart is perfused with Ringer's Solution containing only one-half or one-quarter of the normal amount of calcium, the beneficial effect of adrenaline is then seen at once.

Calcium is absorbed rapidly when taken by mouth, and it may be doubted whether there is ever much justification for injecting it intravenously. Oral administration should always be sufficient. Because calcium is excreted both in the large intestine and in the urine, some have an erroneous impression that calcium administered orally is not absorbed, and that for this reason intravenous injection is necessary. For oral administration calcium lactate is suitable.

Parathyroid Extract and Lead Poisoning.—An injection of parathyroid extract such as parathormone causes a rise of serum calcium by driving calcium out of the bones. Some or all of the calcium so displaced is excreted in the urine and fæces. Tumours of the parathyroid glands accompanied by excessive secretion of the hormone and a rise of serum calcium cause a continuous depletion of the calcium in the bones, which become brittle, and fractures occur. Removal of the tumour causes a drop in the serum calcium to subnormal figures such as 7 mg. per 100 c.c. The normal value is 10–11 per 100 c.c.

In lead poisoning, a disease which commonly occurs among painters and decorators, characterized by anæmia, a blue line on the gums, colic, constipation and peripheral neuritis, shown as "dropped wrist," the lead becomes deposited in the bones. By injection of parathyroid extract the lead can be brought out of the bones in the same way as calcium, and it is then excreted. A series of injections therefore helps to remove the symptoms of poisoning. Some authorities state that when the lead is brought out of the bones into the blood, there is a danger of an exacerbation of the symptoms; others deny this.

Calcium Deficiency.—Calcium deficiency occurs during lactation both in women and in cows. In women it gives rise to osteomalacia, when the bones become thin and porous; this may also occur during pregnancy. In cows the hypocalcæmia is often severe, and the animal becomes comatose.

The Use of Iodine in Medicine.—Iodine is used in medicine for several purposes. It is used (1) as a disinfectant,

(2) in relation to diseases of the thyroid gland, (3) in the treatment of syphilis and (4) as an expectorant. Among people living in districts in which the soil contains less iodine than usual, the incidence of goitre is extremely high. Goitre consists of a swelling of the thyroid gland to many times its normal size. The pathology of goitre was studied by Marine who showed that if the thyroid glands of pregnant bitches were removed, the glands of the offspring were hyperplastic. In a normal thyroid gland the vesicles are full of colloid and are lined with a flattened epithelium. The colloid represents a store of thyroid secretion in excess of requirements. In the hyperplastic gland there is no store of secretion in the vesicles; these are small and empty and lined with active cubical epithelium. The picture of the hyperplastic gland suggests that the cells producing secretion have greatly increased in numbers, and are attempting to manufacture the thyroid secretion without success. Similarly Mellanby found that if bitches are kept during pregnancy on a diet deficient in iodine, then the thyroids of the puppies are enlarged, and those of the third litter are enormous.

In America, in a district in which goitre was prevalent, Marine introduced the prophylactic use of sodium iodide, which was given to school-children eight times a month during two months of the year, up to a total of 4 gm. The results were extremely good, and have been confirmed in other parts of the world. To simplify the administration of the sodium iodide, iodized table salt was introduced, and it was found that congenital goitre, which had previously been present in certain districts in no less than half the children, was prevented by giving this table salt to women during pregnancy. The use of iodized table salt has indeed been adopted so enthusiastically that it is believed to have increased the incidence of hyperthyroidism, and there has been much discussion of the amount of iodide which may safely be put in the salt. The Swiss Goitre Commission recommend 5 parts per million, while Marine proposes 400 times as much. It is clear that in recommending the use of iodized table salt to a patient, the doctor should stipulate how much iodide should be present, and probably 5–10 parts per million is enough.

The story of the pathology of ordinary goitre may be completed by considering the fate of the hyperplastic and en-

larged thyroid glands of puppies born of mothers fed on an iodine-deficient diet. If, when the puppies are still small, iodine is given, the glands then resume the normal histological structure and become small in size. If, instead, iodine is withheld for a year or two, the gland becomes very large; when iodine is then given the gland remains enlarged but the structure is that of a typical colloid goitre as found in patients.

Iodine in Food.—Iodine is present in food only in small amounts. It is chiefly present in fish; thus it is present in cod-liver oil, and it may be that many of the virtues of cod-liver oil are due to the iodine present rather than to other constituents. Pregnant women require about 0·1 mg. iodine daily; this is present in 2 oz. cod-fish, or in 3 teaspoons of cod-liver oil.

Iodides in Syphilis.—In exophthalmic goitre iodides are also used, as will be discussed later. In tertiary syphilis the spirochætes cause the formation of a structure known as a gumma; it may occur for example in the tongue. A gumma is a mass of fibrous tissue in which the living spirochætes are present, but which protects them from the action of anti-syphilitic agents. Potassium iodide is given in doses of 1 gm., three times a day for certain periods; this causes the resolution of the fibrous tissue and exposes the spirochætes to the action of the arsenic compounds.

If 1 gm. potassium iodide is taken by mouth, it causes salivation, lachrymation and running of the nose. It also causes increased bronchial secretion. In all these the potassium iodide is directly excreted by the cells of the glands or mucous membrane. Thus its expectorant action is not produced reflexly by irritation of the vagus nerve endings in the stomach.

Use of Thyroid Gland.—Thyroid powder is prepared from the fresh thyroid gland by removal of connective tissue and fat; the glands are then dried and powdered and fat is removed by extraction with light petroleum. Thyroid is generally stated to be used in the treatment of children born as cretins, who remain mentally and physically undeveloped, and also in the treatment of patients with myxœdema, who are mostly elderly people in whom thyroid deficiency supervenes. In fact patients in these two classes are relatively few, yet thyroid is very much used in medicine. The wide-

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spread use of thyroid may be perhaps most simply explained by saying that thyroid acts as a tonic. Thyroid causes a rise in the basal metabolic rate, and when increased combustion takes place in the body, the patient has more energy. A greater proportion of the food is burnt and a smaller proportion is stored as fat. Minor degrees of thyroid deficiency are sometimes evident in growing children; commonly they occur too in women between the ages of 18 and 35, revealing themselves by the symptoms of loss of appetite, loss of energy, amenorrhœa and by the falling out of hair. Thyroid is one of the few hormone preparations which can be taken by mouth. While thyroxine is often spoken of as the active principle, it probably exists in combination with other amino acids, for when thyroxine is given by mouth it exerts less effect than the same amount of thyroxine in thyroid combination.

Hyperthyroidism.—The condition in which the thyroid is acting excessively is known as exophthalmic goitre. The basal metabolic rate is high, the pulse rate is high, the eyeballs protrude, the thyroid gland pulsates. Histologically the thyroid appears without colloid in the vesicles and with an active cubical epithelium. The patient loses weight, perspires greatly, and is extremely anxious and nervous. In severe cases the treatment is surgical, and a large part of the gland is removed. In preparation for the operation iodine is given in the form of Lugol's solution which contains 2 per cent. iodine dissolved in 3 per cent. potassium iodide. This has the effect of producing a striking improvement in the patient's condition. The basal metabolic rate falls to normal, the pulse rate drops and the body weight rises. This improvement does not persist much more than 14 days, and if the administration is stopped, the patient at once relapses and may be worse than before. Even if the administration is continued the patient cannot maintain the improvement, and therefore the operation is carried out.

In milder cases, when surgical treatment is not considered, the best medical treatment is to send the patient into the country to very quiet surroundings, and to give him 3 pints of milk daily. The large calcium intake has a beneficial effect on the myocardium, diminishing the risk of fibrillation when tachycardia is present for a long time.

CHAPTER XIV

IRON, LIVER EXTRACT AND THE LIVER

Iron in the Food.—The amount of iron entering the body each day in the food is about 15 mg., of which about 10 mg. is available for absorption. There seems, however, to be no active absorption of this iron in healthy individuals, and it is excreted in the fæces. McCance and Widdowson have recently shown that in six subjects examined for 14 days the intake and output were the same to within 2 per cent., and since the estimation of iron in small amounts is difficult, their result can be taken as complete agreement between intake and excretion. In a further experiment in which the six subjects took iron in medicinal form for 14 days, the amount being 7 mg. a day, McCance and Widdowson found that here also the excretion accounted for the extra iron ingested; there was no absorption or storage. When, however, in a third experiment the same amount of iron was injected intravenously, all the injected iron was retained, and none was excreted.

These results indicate that in the normal healthy person the addition of small amounts of iron to the food does not lead to increased absorption, and further that when moderate amounts are injected, they stay in the body, and are not actively excreted by the intestine. The addition of large amounts of iron to the food is, however, followed by absorption and retention of some of the iron. Apparently the passage of iron from the intestine into the blood stream is governed by the concentration in the two places. Only when the concentration in the intestine greatly exceeds that in the tissues does iron pass from the intestines to the tissues. Naturally in persons suffering from iron deficiency the concentration in the tissues is low, and these will for that reason absorb iron more readily. But even so, it is necessary to raise the intake from 10 mg. to 200 mg. per day, in order to obtain a satisfactory uptake of iron by the body. Once, however, the iron is absorbed, it remains in the body and is not excreted.

Iron cannot be given usefully by injection, because of the danger of toxic symptoms. The intravenous injection of so

small an amount as 20 mg. has been known to cause symptoms in unusually sensitive patients, and doses of 80 mg. often produce headache, nausea and vomiting.

Importance of Copper.—In the rat, some copper is necessary for the conversion of inorganic iron into the combination hæmoglobin. In the dog, however, copper is unnecessary, and it may be that it is unnecessary in man. Most medicinal preparations of iron contain small amounts of copper, so that this need not be added; if, however, it is desired to do so, copper is added as copper sulphate in amount not exceeding 2 mg. daily.

Administration of Iron.—Iron is given in the ferrous and ferric forms. The ferrous compounds are the more potent, but they are more inclined to produce gastro-intestinal irritation. In Table IX taken from Witts (1936) is shown the average effective dose of the common preparations of iron, and also the percentage of iron administered which is utilized for hæmoglobin formation.

TABLE IX

PREPARATION.	DAILY DOSE IN GM. OR C.C.	IRON CONTENT IN MG.	UTILIZATION PER CENT.
(*a*) Metallic—			
Ferrum redactum .	1·5–6·0	1200–5000	0·5–2·0
(*b*) Ferrous—			
Ferrous chloride . .	0·25–0·5	100–200	12·5–24
Ferrous sulphate exsic.	0·6	180	14
Ferrous lactate . .	1·5	300	8
Pil. ferri carb. (Blaud)	3·0–4·0	300–400	6–8
(*c*) Ferric—			
Liq. ferri perchlor. .	8·0	400	6
Ferric citrate . .	2·0	400	6
Soluble ferric oxide .	35	1000	2·5
Complex ferric—			
Iron and ammon. cit.	4·0–8·0	800–1600	1·5–3·0
(*d*) Injection—			
Inj. Ferri B.P. 1932	5·0–10·0	16–32	100

Witts has defined the average effective dose as the dose which produces an average increase of over 1 per cent. of

hæmoglobin a day in a sufficiently large sample of patients with achlorhydria and anæmia when the initial hæmoglobin level does not exceed 50 per cent., and when the period of observation is not less than 25 and not more than 40 days. As a convenient prescription Witts recommends

Iron and ammonium citrate 30 *grains*
Glycerine 15 *minims*
Chloroform Water to 1 *oz.*
three times a day after food.

A second is

Pil. ferri carb. 15 *grains*
three times a day after food ;
to be crushed before taking.

A third is

Ferrous chloride 3 *grains*
Syrup 15 *minims*
Chloroform water to 1 *drachm*
to be taken in milk, three times
a day, after food.

Use of Iron in the Body.—After iron is absorbed it is believed to be taken up by the nuclei of the erythroblasts which use it in the formation of hæmoglobin. Iron is also taken up by other cells for the manufacture of cytochrome. The fact that children during the first two years of life are often anæmic, and that women during the years in which menstruation goes on are often anæmic is insufficiently realized and escapes notice. During menstruation about 50 mg. of iron is lost at each period, but in menorrhagia as much as 200 mg. may be lost. During pregnancy an average daily storage of 3·2 mg. iron is required. Hence many anæmias in which the hæmoglobin percentage is low, and which are therefore called hypochromic, are simple nutritional anæmias due to too little iron in the diet. Of foods containing iron liver is the richest, having about 15 mg. per 100 gm.; spinach contains 5 mg. per 100 gm., and meat contains 2–5 mg. per 100 gm.

Pernicious Anæmia.—There are two forms of anæmia, the hypochromic type, and the macrocytic type; in the

second the shortage is not a shortage of hæmoglobin but of corpuscles; the corpuscles which are present are large (macrocytic) and contain more hæmoglobin than a normal corpuscle. The chief anæmia of the macrocytic type is pernicious anæmia; it occurs due to deficiency of an anti-anæmic principle stored in the liver but formed in gastric digestion through the interaction of two factors, (*a*) an enzyme described by Castle present in normal gastric juice, and (*b*) a substance occurring in the diet, often associated with vitamin B_2; it appears to be a product of protein breakdown.

Minot and Murphy first showed (1926) that the administration of liver produced a cure of pernicious anæmia; it caused a rapid rise in the percentage of red cells which contain a reticulum (reticulocytes) indicative of the new formation of corpuscles. Thereafter the number of red cells steadily rose. In 1928 Castle and Locke showed that meat partially digested with gastric juice was curative in action, though gastric juice alone had no effect. One year later it was found that dried hog's stomach was efficient, for it supplied the intrinsic factor absent from the patient's stomach. Since 1 oz. hog's stomach was equivalent to $\frac{1}{2}$ lb. liver, this discovery made the treatment much easier for the patients to tolerate.

Dakin and West have obtained a concentrate, known as anahæmin, of the antianæmic factor in liver which is used for intramuscular injection, and which is given either once in 2, or 4 or 6 weeks as necessary. The dose of the best preparations which produces a maximal response varies from 30–60 mg. The treatment must be prolonged, for unless a normal red cell count and a normal hæmoglobin value is restored there is a danger of a development of lesions of the spinal cord.

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CHAPTER XV

DISINFECTANTS

The Halogens.—Both chlorine and iodine are much used as disinfectants. Chlorine is liberated from bleaching powder, which is chloride of lime, and it is also liberated from the corresponding sodium compound, which is sodium hypochlorite; this is the active constituent of the proprietary solution Milton. The important fact about chlorine is that it is inactivated by organic matter and therefore it is of no value for disinfecting a water-closet. On the other hand, when little organic matter is present, as for example in the water of a swimming-bath, chlorine is a good disinfectant and will act in a dilution of 1 in 2·5 millions. When chlorine is used to disinfect a wound, it is applied in the form of eusol or Dakin's solution; so soon as the chlorine is liberated it combines with the proteins in the exudate from the wound and is inactivated. The wound should therefore be given continuous irrigation with the solution. Dakin's solution is Liquor Sodæ Chlorinatæ Chirurgicalis B.P.; it is prepared from chlorinated lime, sodium carbonate and boric acid, and contains about 0·5 per cent. of available chlorine. It is less irritant than eusol. Certain organic compounds of chlorine, the chloramines and azochloramid are said to retain some activity in the presence of organic matter.

Similar considerations hold good for iodine. Thus iodine is an excellent disinfectant for the intact skin but it is not much good for a wound, since its disinfectant power is destroyed by blood or serum.

Oxidizing Agents.—Potassium permanganate and hydrogen peroxide belong to the class of disinfectants which are oxidizing agents. They are less irritant than the halogen class, but like the members of this class they are inactivated by organic matter. Thus the presence of blood greatly reduces the efficiency of both potassium permanganate and of hydrogen peroxide.

Salts of the Heavy Metals.—The best-known disinfectants in this class are the salts of mercury. Their action is exerted very slowly and therefore they are of no use where a rapid disinfection is desired; they combine with serum proteins

and must therefore be used outside the body. Bacteria apparently killed by mercuric chloride resume growth when placed in a medium containing blood. Mercury biniodide is less irritant than mercuric chloride, but it is also less efficient. Mercurochrome, which stains tissues red, and which is relatively non-toxic, has gained great popularity, though this is now declining. First introduced as an antiseptic for the urinary tract, it was later recommended for septicæmia. In fact its bactericidal action is very small, and it is relatively inefficient. Phenyl mercuric nitrate, metaphen and merthiolate are much better disinfectants than mercuric chloride, but they are inactivated by serum proteins and also by blood. Metaphen is the anhydride of 4-nitro-5-hydroxymercuric-o-cresol; it is used for disinfecting skin and instruments. Merthiolate is sodium ethyl mercurithiosalicylate; in a strength of 1 in 10,000 it is useful as a preservative for vaccines and serums.

Coal-tar Derivatives.—The fourth group of disinfectants are the coal-tar disinfectants. The distillation of coal-tar yields a series of compounds the first of which is phenol; this is soluble in water, bactericidal and exceedingly poisonous. As the temperature of distillation is raised other products are obtained of which the batericidal power is greater, but the toxicity and the solubility are less. The products of distillation may therefore be divided into two classes:

(*a*) Phenols and cresols, which are too caustic for use in the body,

(*b*) Emulsions of tar acids, such as izal and cyllin, which are more bactericidal but less caustic. Dettol is a pure substance of this class, combined with chlorine (*p*-chlor-*m*-xylenol); it is bland and may even be used undiluted.

The great and important advantage of the coal-tar disinfectants is that they are not so much affected by the presence of organic matter. The bactericidal action of phenols and cresols is well maintained in the presence of organic matter, and though the activity of the emulsions of tar acids is depressed by organic matter, this depression is not very great, and in suitable concentrations they are active in the presence of blood and serum.

Dyes.—The fifth class of disinfectants is the class of dyes of which the most important group is the acridine series, with acriflavine as the best-known member. Acriflavine, which

is a dye giving a yellow solution, and used in a concentration varying from 1–500 to 1–3000, is an excellent prophylactic against wound infections. If an emergency operation has to be carried out in circumstances in which asepsis is impossible to attain, then the correct disinfectant to use is acriflavine. The presence of serum or blood so far from neutralizing its action, intensifies it. The abdominal cavity may, for example, be washed out with a solution of acriflavine, for it is non-toxic and does not kill leucocytes. Tissues may be infiltrated with acriflavine.

It has recently been shown that acriflavine is unsuitable for application to the brain, as it produces hæmorrhages and necrosis. Proflavine sulphate, which is a well-defined chemical compound closely related to acriflavine, does not suffer from this disadvantage. It is likely that proflavine sulphate will gradually replace acriflavine altogether, as it is equally efficient.

Antisepsis in Midwifery.—Much attention has been given to the antisepsis in midwifery since it has been demonstrated by Colebrook that puerperal septicæmia is due to a hæmolytic streptococcus belonging to group A, not normally present in the vagina, and therefore introduced from outside. In view of this finding the sterilization of the hands is of great importance, for doctors may easily infect the patient in the course of vaginal examinations. Washing is often combined with the use of antiseptics, and the double operation is believed to render the hands sterile. Colebrook and Maxted (1936) have found, however, that after washing the hands perfunctorily for 20–30 seconds, followed by dipping them in mercuric chloride 1 in 1000, or lysol 1 in 320 for 30 seconds, more than 4000 colonies of hæmolytic streptococci could be grown from a single finger previously infected. In other experiments they examined the effect of washing which would be considered thorough, namely washing with soap and water for 2–3 minutes followed by soaking in lysol, 1–160, for 3 minutes. It was found that though the hæmolytic streptococci, previously placed on the fingers, were greatly reduced in numbers, they were still present. Curiously enough washing the hands with yellow soap and warm water for 5 minutes was able to destroy all streptococci and organisms not normally present on the skin. Staphylococci and diphtheroids were however not reduced at all, and were still present, though in smaller num-

bers, if after this washing the hands were placed in mercuric chloride, 1–1000, for 3 minutes.

None of these procedures, however, completely sterilized the hands, and more important still, they failed to leave the skin protected against later contamination. Colebrook and Maxted tested a number of disinfectant substances to see whether they left the skin bactericidal afterwards. They obtained the results given in Table X.

TABLE X

	INTERVAL BETWEEN TREATMENT BY ANTISEPTIC AND INFECTION OF SKIN BY STREPTOCOCCI.	NO. OF STREPTOCOCCAL COLONIES GROWN FROM	
		SKIN AREA TREATED BY ANTISEPTICS.	UNTREATED (CONTROL) AREA.
Carbolic soap . . .	10 minutes	17,600	not done
Ether soap followed by surgical spirit . .	10 ,,	800,000	not done
Mercuric chloride (1 in 1000)	30 ,,	1,000	10,000 (approx.)
Lysol (1–160)	30 ,,	5,280	8,000
Brilliant green and crystal violet (1 in 200) .	30 ,,	320,000	—
Iodine (2 per cent. with 4 per cent. pot. iod. in water)	6 hours	nil	41,600
Dettol (undiluted) .	5 ,,	nil	1,900,000
Dettol cream (30 per cent.)	3 ,,	nil	600,000

The results in Table X show that the efficient skin antiseptics are iodine and dettol, for these leave a skin which is actively bactericidal. Dettol cream appears to be a very useful product; it contains 30 per cent. dettol in gum tragacanth. When rubber gloves are worn, they can be given a bactericidal surface by covering them with a layer of dettol cream.

Sterilization of the Skin for Surgery.—Having discussed the special problems which arise in midwifery, we may now

turn to the use of disinfectants in surgery. In preparing the skin for an operation, it is first cleaned with ether soap and water and dried with spirit. For the purpose of disinfection, which is not secured by this cleaning, iodine is often used; iodine suffers from the drawback that it is irritant to some skins, and further that its action is destroyed by contact with blood. Picric acid is also used, but this is also irritating to some skins, and it may be absorbed and cause poisoning. The most satisfactory substances which penetrate the superficial layers of the skin and have a persistent action are:

(*a*) Tinker and Sutton's solution: 5 per cent. acriflavine, 10 per cent. acetone, in 50 per cent. alcohol.

(*b*) Bonney's blue paint: 0·5 per cent. brilliant green, 0·5 per cent. crystal violet, in 50 per cent. alcohol.

(c) Harrington's solution: mercuric chloride 0·8 gm., hydrochloric acid 60 c.c., methylated spirit 640 c.c., water 320 c.c.

Sterilization of Wounds.—The disinfection of wounds has been revolutionized by the introduction of sulphanilamide, which has been shown to be highly effective. Sulphanilamide, which is much the most soluble compound, is the one which should always be used, and sulphapyridine or sulphathiazole are much inferior being so much less soluble. Statements are made that sulphadiazine is a good wound disinfectant, but as this substance also has a very low solubility, they should be received with caution. Sulphanilamide is applied to wounds as a fine powder. Pastes consisting of sulphanilamide and cod-liver oil have also been introduced, but clinical reports so far are few. If sulphanilamide is not available disinfectants of the diamino acridine series like acriflavine are the best. A dressing saturated in 0·2 per cent. acriflavine may be applied for 2 hours, or if the wound is caused by a puncture the acriflavine injected. Other suitable solutions are 5 per cent. dettol, 0·5 per cent. izal, or 0·5 per cent. cyllin.

The irrigation of infected wounds with Dakin's solution is very often satisfactory because it (*a*) cleanses, (*b*) deodorizes, (*c*) promotes fluid exudation by a slight irritant action and (*d*) prevents the access of further infection.

Disinfection of Materials.—For the disinfection of utensils and furniture it should be remembered that lysol is twice as potent as phenol and is half the cost. Lysol in

strength 2 per cent. is therefore about as efficient as 5 per cent. phenol. Izal or Jeyes' fluid in 1 per cent. solution can also be used.

For sterilizing instruments the use of alcohol alone is not enough, for its bactericidal action is doubtful; it is best at a strength of 70 per cent. A mixture of 1 part of lysol and 3 parts of alcohol is the best.

For sterilizing catheters, either a solution of mercuric chloride (1 in 1000), in which they are left for one hour, or dettol is employed.

The sterilization of catgut is a procedure demanding much experience; the difficulty arises from the presence of spores inside the gut which cannot be destroyed by disinfectants, but can only be killed by heating to 150° C. for one hour. This process of heating damages the gut, and only those who have had much practice can carry out the sterilization satisfactorily. Sometimes catgut is sold as "partially sterilized," for which it is claimed that the spores inside have been destroyed, so that the surface only remains to be sterilized. This can be done by soaking the gut in a solution of 1 per cent. iodine in 1·5 per cent. potassium iodide solution for 10 days, but the soaking reduces the tensile strength of the gut. It is preferable that gut should always be purchased in a completely sterile form. Its manufacture is controlled in Great Britain by the Therapeutic Substances Act which ensures above all that only those manufacture catgut who are properly trained for the work.

CHAPTER XVI

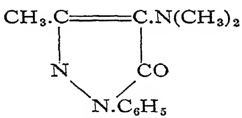
ANALGESICS AND ANTIPYRETICS

The Treatment of Fever.—A rise of body temperature above the normal level is due to an increase in heat production often accompanied by shivering and vasoconstriction in the skin; there is a reduction in blood volume. When children have a high temperature they should be given sodium citrate and fluids. In the body the citrate is oxidized to carbonate;

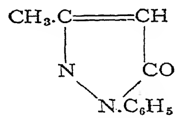
the excretion of carbonate in the urine makes the urine alkaline. The purpose of giving sodium citrate is that this by itself sometimes reduces the temperature. When adults have a high temperature they should also be given sodium citrate with plenty of fluids, for this diminishes the risk of infection of the urinary tract.

Apart from these measures, it is rarely desirable to use drugs to reduce body temperature unless the temperature is so high that the patient becomes delirious. Probably the best method even then is to reduce the temperature by sponging with tepid water, or by a bath at 25° C. for 10 minutes, after which the patient is lifted on to a sheet and wrapped in blankets; or again the patient may be given a wet pack, when he is wrapped in a sheet wrung out in water at 20° C. Two blankets are then wrapped round the sheet and the patient is left for one hour. The use of baths and packs is too little known and practised.

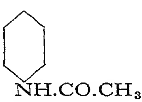
Antipyretic Drugs.—Antipyretic drugs do not cause a fall of temperature in health, but only when the temperature is raised. The best-known of these are amidopyrin, phenazone or antipyrin, acetanilide, phenacetin and aspirin. The formulæ of these are given below.



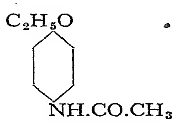
Amidopyrin



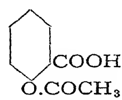
Phenazone



Acetanilide



Phenacetin



Aspirin

The relative efficiency of these different substances has been determined by Brownlee in cats in which pyrexia was produced by the injection of a culture, previously killed, of

Bacillus coli, and also in rats in which pyrexia was produced by the injection of a suspension of dried yeast. The results in the two species were similar as shown in Table XI.

TABLE XI

	Equivalent anti-pyretic doses; mg. per kg.		Mean lethal dose; gm. per kg.	Ratio lethal anti-pyretic.	Relative anti-pyretic potency.
	Cats.	Rats.	Rats.	Rats.	Rats.
Acetanilide .	16·5	24	0·82	35	166
Amidopyrin .	25	31	1·15	37	129
Phenacetin .	33	40	1·25	31	100
Phenazone .	33	40	1·53	38	100
Aspirin . .	54	54	1·24	23	74

The last column of Table XI shows that if the value 100 is given to phenacetin, then phenazone is similar in activity, while amidopyrin and acetanilide are more potent, having the values of 129 and 166 respectively; aspirin is less potent with the value of 74. On these figures it is difficult to account for the great popularity of aspirin, especially in view of the fact that for rats the ratio of the lethal to the antipyretic dose is lower for aspirin than for the other substances.

The safety of aspirin probably depends on the fact that it does not produce agranulocytosis. This is a condition in which the polymorphonuclear leucocytes disappear from the blood stream or become very few, and in which resistance to disease therefore falls very low. Agranulocytosis has been shown beyond question to occur after the use of amidopyrin, though the incidence of agranulocytosis among persons taking amidopyrin must be very low indeed. The similarity of the structure of phenazone to that of amidopyrin makes it likely that phenazone will also produce agranulocytosis, though this has not so far been described. Acetanilide and phenacetin being simple derivatives of aniline, like sulphanilamide, may be expected to produce similar toxic effects.

Acetanilide is known to produce methæmoglobinæmia, and may occasionally produce agranulocytosis. Phenacetin is believed to be less dangerous, but in view of its structure it is difficult to see why this should be so.

Aspirin has had a widespread use in recent years, and remarkably few toxic effects have been described; it is commonly used as an analgesic rather than as an antipyretic, and the two properties may not be proportional. Thus the figures in Table XI may be no guide to the value of the different substances as analgesics, for relief of headache, toothache and vague rheumatic pains.

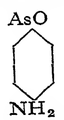
The Use of Salicylates.—Sodium salicylate is used in the treatment of acute rheumatic fever, which is a disease of early life rarely seen after the age of 25. It is characterized by high temperature with one or more joints inflamed, swollen and intensely painful. Sodium salicylate is given in doses of 1·3 gm. (20 gr.) every two hours, together with the same amount of sodium bicarbonate. The maximum daily amount is 12 gm. Usually the temperature and joint pains are reduced in 48 hours. This dosage of sodium salicylate is large and produces in some people toxic effects such as vomiting, headache, deafness and sweating. There is however a very wide variation in the susceptibility of different persons to sodium salicylate, some tolerating not more than 40 gr., and others as much as 470 gr. In children the maximum daily dose is 4 gm. (60 gr.). Salicylic acid is excreted in the urine in combination with glycine, as salicyluric acid.

The Treatment of Gout.—In gout, deposition of urates occurs in the body. By the use of 2-phenylquinoline-4-carboxylic acid the threshold at which the kidney excretes uric acid is lowered, and much uric acid is excreted. This substance is known by various names, cinchophen, quinophan, atophan, agotan; its use is not without danger, for it can produce toxic symptoms, loss of appetite, nausea, vomiting and jaundice. Death from acute yellow atrophy has been known to occur. Cinchophen must therefore be given only when the patient is closely supervised.

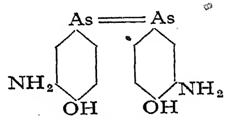
CHAPTER XVII

THE ORGANIC ARSENICAL COMPOUNDS, MERCURY AND BISMUTH

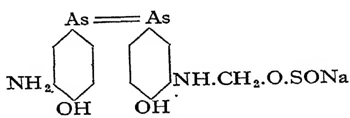
The Introduction of Salvarsan.—The value of arsenic for the treatment of protozoal diseases was shown in 1902 by Laveran and Mesnil who found that sodium arsenite killed trypanosomes. Thomas in 1906 showed that when $-AsO(OH)_2$ was linked to the dye aniline, the substance formed, which he called atoxyl, would cure trypanosomiasis in rats. The conception of using a dye as a trypanocidal substance was, however, due to Ehrlich, who had shown in 1904 that trypan red would kill trypanosomes. Ehrlich later investigated the arsenical derivatives of aniline thoroughly. Pentavalent compounds like atoxyl, although active in animals, had no effect in vitro, and he was thus led to concentrate on the trivalent compounds.



Arsenoxide



Arsphenamine



Neoarsphenamine

The arsenoxide derivative was too toxic for therapeutic purposes, though it was powerfully trypanocidal. Salvarsan or Arsphenamine was found to be satisfactory, but it was stable only as an acid salt. For injection it was necessary to dissolve it in a large volume of water and convert it to the base by the addition of sodium hydroxide.

Neoarsphenamine and Sulpharsphenamine.—To avoid the disadvantage of injecting a large volume, neoarsphenamine was introduced, which is a condensation product of arsphena-

mine and sodium formaldehyde sulphoxylate. For the treatment of syphilis it is injected in a 6 per cent. solution, in a dose varying from 0·3–0·9 gm., and usually 0·45 or 0·6 gm. The solution must be prepared not only in distilled water, but in water which has been freshly distilled. Moreover, the solution once prepared must be injected at once, for even if not shaken, and if kept in a stoppered vessel, contact with air above the solution causes it to increase in toxicity by 20 per cent. in 20 minutes. Substances like arsphenamine and neoarsphenamine act in the body by breaking down to the arsenoxide form. Neoarsphenamine is sold under the names Novarsenobillon and Neokharsivan.

A third compound of this type is sulpharsphenamine which has the advantage that it need not be given by intravenous injection, but can also be given by intramuscular injection. Sulpharsphenamine is sold as Sulpharsenol and as Kharsulphan. Neither neoarsphenamine nor sulpharsphenamine as usually prepared are pure chemical substances and are therefore tested by biological methods to ensure (*a*) that their toxicity does not exceed a certain limit, (*b*) that their potency does not fall below a certain limit.

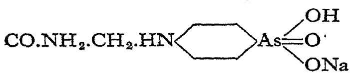
A fourth compound containing trivalent arsenic is arsphenamine di-glucoside, sold as Stabilarsan. Each NH_2 of arsphenamine is combined with a molecule of glucose with the loss of H_2O. This substance is stable in solution and can be injected without preparation.

Treatment of Syphilis.—Ehrlich's aim in introducing salvarsan and neosalvarsan was to find an agent which would cure when given as a single injection. Neosalvarsan, or neoarsphenamine, is successful in doing this in relapsing fever. In syphilis, however, a long course of treatment is needed. A common procedure is to give one intravenous injection of neoarsphenamine weekly for 10 weeks together with bismuth by intramuscular injection. There is then an interval of 4 weeks when potassium iodide is given in a dose of 1 gm. three times a day. A period of 14 weeks is thus covered. The whole treatment is then repeated four times. The usual total dose of neoarsphenamine in 10 weeks is 6 gm., and of bismuth 3 gm.

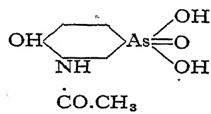
Toxic Symptoms of Organic Arsenicals.—Toxic symptoms are of two classes, immediate reactions and later

reactions. The immediate reactions are headache, vomiting, rigors and fainting. There may be a sudden fall of blood pressure described as a nitritoid crisis, because the effect resembles the effect of taking nitrites which dilate the arterioles. Such an attack is arrested by the prompt injection of adrenaline (0·5 c.c. of 1 in 1000). Later reactions, occurring after the 2nd or 3rd injection, are due to arsenical poisoning; they are skin reactions, usually an exfoliative dermatitis; or there may be jaundice and acute yellow atrophy of the liver.

Pentavalent Arsenical Compounds.—The first pentavalent arsenical compound was atoxyl, but this is now almost never used because it is liable to cause optic atrophy. Two important compounds of this class are tryparsamide and stovarsol.



Tryparsamide



Stovarsol

The pentavalent arsenical compounds having only one benzene ring consists of much less cumbersome molecules than the trivalent compounds. As a consequence of this the pentavalent compounds can penetrate where the trivalent cannot. Thus tryparsamide is used in cerebral syphilis, because it can get into the cerebrospinal fluid. Similarly stovarsol can be given by mouth, since it is able to be absorbed by the gut and to enter the blood stream. The greater diffusibility of the pentavalent compounds also causes them to be excreted by the kidney far more rapidly than the trivalent compounds. In France stovarsol is used as a prophylactic against syphilis. It is also used in the treatment of amœbic dysentery. A derivative of stovarsol known as acetylarsan is given by intramuscular injection in the treatment of infantile syphilis. The pentavalent arsenical compounds are used in the treatment of sleeping sickness rather than the trivalent compounds.

Treatment of Cerebral Syphilis.—In the treatment of cerebral syphilis, injections of 3 gm. of tryparsamide are given once a week for 2 months, and a cure is obtained when the

Wassermann reaction becomes permanently negative. Cerebral syphilis is very difficult to cure because of the inaccessibility of the spirochætes, and treatment with malaria infection has had many good results. The patient is injected with 2 c.c. blood from another patient suffering from tertian malaria; after one or two weeks, paroxysms of malaria occur in which the body temperature rises to a height at which the spirochætes die. Six of these paroxysms are allowed to occur, and then a course of quinine administration is begun by which the malarial parasites are killed.

Action of Inorganic Arsenic.—Arsenic has been much used as a poison because of its sweet taste; it is, however, a severe irritant to the gastro-intestinal tract, producing epigastric pain, vomiting and diarrhœa. If this continues the patient feels cold and becomes collapsed; the pulse becomes weak; after twenty-four hours there is a toxic effect on the heart, liver and kidneys.

When small doses are given frequently, chronic poisoning occurs without the acute gastro-intestinal symptoms just described. Often the first sign is a loss of power in the legs and disturbances of sensation due to peripheral neuritis; there is also pigmentation of the skin. Arsenic is deposited in the hair and in the nails, where it can be detected.

The Use of Mercury in Syphilis.—The use of mercury for the treatment of syphilis is known to go back to the fifteenth century. The effect it produces on the spirochætes is slow in onset, but prolonged. Since mercury is excreted by the kidney, and since it has a toxic action on the kidney, treatment with mercury is not without danger.

Mercury is administered by mouth, or by inunction, or by intramuscular injection. For oral administration a daily dose of 20 mg. mercuric iodide is given. This is convenient for the patient, but it causes gastro-intestinal disturbances and diarrhœa. For inunction mercury ointment, consisting of mercury 300 parts, suet 50 parts and lard 650 parts is used; it is surprising that when so applied mercury is quickly absorbed; it appears in the urine in 24 hours. The body can be saturated in 2 weeks. For intramuscular injection different preparations are used; an injection which is not painful is a suspension of mercury salicylate in oil; a second injection, which although efficient is painful, consists of

calomel 5 per cent., creosote 10 per cent., camphor 10 per cent., in olive oil and wool fat. Those who have had long experience in the treatment of syphilis consider that it is essential to combine either mercury or bismuth treatment with the administration of organic arsenical compounds, for otherwise the percentage of patients who relapse is much greater.

Early signs of mercury poisoning are salivation and gingivitis; in acute poisoning there is nephritis with albuminuria and hæmaturia; casts are present in the urine.

Bismuth in the Treatment of Syphilis.—Bismuth is now replacing mercury. The compounds of bismuth are interesting because of peculiarities in their absorption. From the intestine bismuth salts are not absorbed at all, for the soluble salts are converted into insoluble powders. From intramuscular injection the absorption into the blood stream is also very slow; thus while a dose of 5 mg. per kg. potassium bismuth tartrate will kill a rabbit if given intravenously, as much as 200 mg. per kg. must be given to cause death after intramuscular injection. This difference is astonishing, for there is little difference between intramuscular and intravenous injection for most inorganic substances. In syphilis metallic bismuth suspended either in water or in oil is injected intramuscularly; the bismuth becomes encapsulated and forms a depot from which small amounts of bismuth are constantly liberated into the blood. The toxic symptoms of bismuth are similar to those of mercury.

CHAPTER XVIII

THE TREATMENT OF MALARIA, TROPICAL DISEASES AND WORM INFECTIONS

The Malaria Parasite.—The malaria parasite invades the human being when an infected mosquito bites. The forms of parasite which are first present in man are known as sickle forms. They invade the red corpuscles, and there they undergo asexual reproduction by division. Inside the

corpuscle the asexual forms of the parasite are known as schizonts. At intervals of 48 or 72 hours, according to the species of parasite, the schizonts burst out of the corpuscle and are free in the blood; it is at this point that the malarial paroxysm with rise of body temperature takes place. The liberated schizonts then invade other corpuscles and the reproduction goes further, paroxysms of malaria occurring in the patient every second or third day. The two drugs which act upon the schizonts are quinine and atebrin. If as a result of the presence of quinine in the blood the asexual reproduction cannot be continued, gametocytes are found, that is to say male and female forms. These cannot conjugate in the body, but they do so in the body of the mosquito. Hence if an uninfected mosquito bites a man in whose blood the gametocytes are present, the mosquito becomes infected. Men in whom gametocytes are present are malaria carriers; they are persons who through taking quinine or other means have acquired sufficient resistance to prevent asexual reproduction occurring inside them. The drug which acts upon and kills the gametocytes of malignant tertian is pamaquin B.P. (plasmoquin).

There are different species of malaria parasite: Plasmodium vivax causes benign tertian malaria—it has a 48-hour cycle; Plasmodium falciparum causes malignant tertian, and has a 48-hour cycle; Plasmodium malariæ causes quartan malaria and has a 72-hour cycle.

Quinine.—Quinine is an alkaloid obtained from cinchona bark; it consists of a quinoline ring linked to a piperidine ring by the group -CH(OH)-. It is used in medicine as an antipyretic to prevent the onset of fever; it is believed to act by reducing heat production in contrast to other antipyretics like aspirin which act by increasing heat loss. Quinine is much used as a bitter, to increase the flow of gastric juice, the action of quinine being exerted on the nerve endings in the mouth. Quinine has also a reputation as a spermatocide and as an abortifacient, but in fact it has little action on spermatozoa compared with many other substances, and it has little, if any, action on the uterus.

In treating malaria, the full course of quinine is to take 1 gm. (15 gr.) daily for two weeks, and then 0·6 gm. (10 gr.) daily for eight weeks. Malaria is easily cured if treatment is begun as soon as the disease is contracted, as for example when

patients are infected with malaria to cure cerebral syphilis, but when the disease has had a longer hold, many patients relapse. As a prophylactic against malaria quinine is very efficient but must be continued. Thus seamen in ships leaving England and calling at a West African port must take quinine as soon as they call at that port and continue until they return to England. Often they cease to take quinine when they leave the last port on their way home, with the result that they have a malarial attack.

In many people quinine produces toxic symptoms which are in the main sensory disturbances, ringing in the ears and deafness, photophobia and temporary blindness. Quinine is excreted almost entirely in the urine. The toxic effects of quinine, though unpleasant, do not result in permanent damage, and for this reason quinine is a safe drug which can be used freely by persons of little experience. The toxic effects of pamaquin and of atebrin are much more serious.

Pamaquin.—Pamaquin is a synthetic substance produced by Schulemann and Roehl which resembles quinine in being a quinoline derivative. It acts on the gametocytes, and is therefore used in combination with quinine. The combination is valuable in the treatment of malignant tertian malaria in which many gametocytes are present. A dose of 10 mg. or $\frac{1}{6}$ gr. is given three times a day. Larger doses have toxic effects such as cyanosis and formation of methæmoglobin.

Atebrin.—Atebrin is a yellow dye also introduced by Schulemann. Like quinine it acts on the schizonts; it is given in doses of 0·1 gm. or 1·5 gr. three times a day. Atebrin musonate is a soluble form which can be injected either intramuscularly or intravenously. Toxic effects with atebrin are rare but severe. Atebrin is excreted very slowly and may remain in the body for 6–9 months. The toxic action is usually exerted on the liver and in addition there is often a yellow discoloration of the skin which is not surprising in view of the similarity of the chemical structure to acriflavine.

Totaquine.—One of the difficulties of treating malaria is that there are so many patients that the cost of the treatment is an important consideration. Cheaper than quinine is a mixture of the cinchona alkaloids, and totaquine is a mixture which, according to British Pharmacopœia 1932, contains not

less than 70 per cent. of crystallizable cinchona alkaloids of which not less than one-fifth is quinine. Totaquine is more irritant to the stomach than quinine but is believed by many to be not less efficient.

Sleeping Sickness.—Mention has already been made of the use of arsenical derivatives for the treatment of trypanosomiasis, and that the pentavalent compounds are chiefly used. In 1920 a substance known as "Bayer 205" was introduced, which has since been called Germanin. Moranyl is believed to be the same substance. It is related to trypan red and has a very large and cumbersome molecule; from this fact its properties can be deduced. Once it is introduced into the body it cannot get out, consequently a single injection produces a prolonged immunity to infection; it does not alleviate patients in whom the cerebrospinal fluid is infected, but is efficient in the earlier stages of the disease; it occasionally produces toxic effects on the kidneys.

Amœbic Dysentery.—This form of dysentery is due to infection of the intestinal tract with the Entamœba histolytica which ulcerates the intestine. Ipecacuanha root has long been used in the treatment of this disease, and owes its activity to the alkaloid emetine. Emetine, as its name implies, is intensely irritant to the stomach and produces vomiting; for this reason emetine cannot be given by mouth, but is injected under the skin as hydrochloride. Since emetine is excreted into the alimentary tract, some irritant action remains even after subcutaneous injection. A full course of treatment is to give 30 mg. ($\frac{1}{2}$ gr.) emetine hydrochloride twice a day for 10 days; by this means a complete cure can be obtained and the patient prevented from becoming chronically infected.

Emetine bismuth iodide is a compound of emetine which can be given by mouth since it is insoluble in water and dissolves in the intestine very slowly. In the treatment of chronic cases it is stated to be efficient.

Emetine is excreted slowly, and therefore accumulates in the body; it has a toxic action on the heart muscle, and therefore careful observation of the patient is necessary during a course of treatment.

That stovarsol is used in the treatment of amœbic dysentery has already been mentioned, but a similar substance, car-

barsone, is stated to be preferable because it is not so toxic. Yatren, which is also used, is a quinoline derivative.

Leishmaniasis.—This disease exists in the two forms kala-azar and oriental sore. It is treated by antimony compounds, which may be either tartar emetic or organic antimony compounds. Antimony compounds are, as might be expected, in many ways similar to arsenic compounds, with the important difference that antimony is much more readily excreted. Antimony was at one time used in trypanosomiasis, but it has now been replaced by tryparsamide ; this is probably because the antimony stays in the body for too short a time.

Pentavalent organic compounds such as urea stibamine are said to be the most efficient, but they are expensive. For the treatment of kala-azar a 2 per cent. solution of potassium antimonyl tartrate is injected intravenously twice weekly, and continued until 2 gm. have been given.

Recently stilbamidine, or diamidinostilbene, has been used successfully in leishmaniasis. This substance was introduced as a treatment for trypanosomiasis as a result of the discovery that synthalin had a toxic action on typanosomes. Trypanosomes depend for their survival in vitro on liberal amounts of dextrose, and synthalin was tried in trypanosomiasis because it is known to cause a fall in blood sugar. Synthalin is a derivative of guanidine in which two guanidine groups are connected by a long $—CH_2—$ chain. Synthalin was found to cure trypanosomiasis, though not because of its action on the blood sugar. In stilbamidine the guanidine groups of the synthalin chain are connected by two benzene rings with $—CH : CH—$ between the rings. Stilbamidine has been very effective in the treatment of leishmaniasis.

Bilharziasis.—Bilharziasis, also known as schistosomiasis, is a disease due to a worm which lives in the portal veins. This worm lays eggs which are excreted through the mucous membrane of the rectum and of the bladder, and the ova are readily recognized in the urine. The disease is very prevalent among agricultural workers in Egypt. Bilharziasis is treated by the intravenous injection of a 6 per cent. solution of tartar emetic. Tartar emetic cannot be given by mouth because it produces vomiting. Since the antimony is rapidly excreted from the body, repeated injections have to be made ; as a rule the first dose is 60 mg. (1 gr.) followed by doses of

120 mg. every other day until a total of 2 gm. (30 gr.) has been given. For success in treatment it is essential that the parent worm is killed, and this can be detected from the ova in the urine; when no living ova are seen the parent worm is dead.

Ankylostomiasis.—Ankylostoma duodenale is the hookworm which lives in the duodenum. By means of a hook in its mouth, it anchors itself on to the duodenal mucous membrane. Hookworm infection is widespread, and it has been stated that no less than one quarter of the world's population suffers from hookworm. The remedy most extensively used for treatment is carbon tetrachloride, a substance very closely related in composition to chloroform, and having similar toxic effects. Carbon tetrachloride is given by mouth in a dose of 2·5 c.c. or 40 minims. It must be free from carbon bisulphide as impurity, but even when pure toxic effects such as jaundice and fatty degeneration of the liver occasionally follow administration of the therapeutic dose. Persons addicted to alcohol are specially sensitive to the toxic action, and alcohol must never be taken before or after treatment. Administration of calcium lactate increases the resistance to toxic effects.

A second remedy used in the hookworm disease is thymol, which is given in the following way. The patient is kept without food for 12 hours in order to empty the intestine and expose the hookworms to the action of the drug. A purge is then given. Thymol is then given as a fine powder mixed with cane sugar; it should not be put in a capsule or it may be excreted unchanged. The dose is 2–4 gm. (30–60 gr.). Two hours later a second purge is given to remove the dead worms. The efficacy of treatment is judged by examination of the fæces for ova. The treatment may be repeated weekly if necessary.

A third remedy for hookworm disease is Oil of Chenopodium, of which the chief constituent is ascaridole. The advantage of Oil of Chenopodium is that it is unnecessary to prepare the patient by preliminary starvation or by giving a purge, though of course food must not be taken when the oil is acting. The usual treatment is to give three doses of 0·5 c.c. Oil of Chenopodium at intervals of an hour, and then to give a dose of Epsom salts two hours after the last dose.

Tapeworm Infections.—Tapeworms, such as tænia and bothriocephalus, are treated with liquid extract of male fern, which contains filicic acid as its most important constituent. Pure filicic acid is toxic and cannot be given alone; in the extract it is mixed with resins, and so is not so free to be absorbed. Absorption is assisted by the use of oils, hence when extract of male fern is used, castor oil must not be given as a purgative. The toxic symptoms which occur are vomiting and diarrhœa, coma and convulsions. The usual routine in the treatment of tapeworms is to starve the patient for 12 hours, and then to give a preliminary saline purge in the morning. The extract of male fern is then given in a dose of 90 minims (6 c.c.), and two hours later a second saline purge is given. The stools must be kept and carefully examined to see if the head of the worm has been passed, for unless this has happened the worm grows again. To find large portions of the worm in the stools is not sufficient.

Pelletierine tannate is also used in the treatment of tapeworm infections.

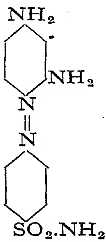
Round Worm Infections.—Infection with round worms (Ascaris lumbricoides) is treated with santonin, which is a derivative of naphthalene. The santonin is usually given with calomel at night and followed by a saline purgative in the morning. The dose is 0·2 gm. or 3 gr., and about one-third of this for a child. Larger doses are dangerous because santonin is absorbed from the intestine and produces visual disturbances (yellow sight), nausea and vomiting.

Threadworm Infections.—Infection with Oxyuris is the commonest worm infection in this country; it rarely occurs in healthy children, but is common in poor health. The worms live in the rectum and can be removed by giving enemata of salt and water, or enemata containing quassia. When infection persists, it is generally because the child re-infects itself. During the night the worms cause itching at the anus and the child scratches. The eggs then get under the finger nails and are then carried to the mouth. Sometimes it is necessary to sew up the night clothes so that the child cannot re-infect itself in this way. In severe cases santonin is given. Diphenan, which is the carbamic acid ester of *p*-hydroxydiphenylmethane, is also used for oxyuriasis. The dose is 0·5 gm. or 7·5 gr. three times daily for one week.

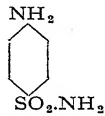
CHAPTER XIX

THE TREATMENT OF BACTERIAL INFECTIONS

The Introduction of Prontosil.—Although much progress has been made in the last 35 years with the treatment of protozoal infections, little success has attended the treatment of bacterial infections by chemo-therapeutic means. In 1935, however, Domagk described the bactericidal properties of prontosil, which he found would protect mice from the



Prontosil



Sulphanilamide

lethal effect of hæmolytic streptococci. Tréfouël, Nitti and Bovet suspected that the protective action of prontosil might be due to the breaking down of prontosil in the body into sulphanilamide, and they found on investigation that sulphanilamide was actually of great bactericidal potency.

Derivatives of Aniline.—We may note in the first place that the introduction of prontosil and sulphanilamide was due to experiments carried out on mice, just as the introduction of the organic arsenical compounds was due to experiments on mice.

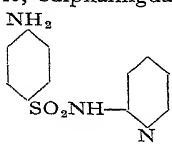
That so simple a substance as sulphanilamide should be bactericidal is especially interesting because of its relation to the dye aniline. The beginning of the organic arsenical compounds was the introduction of atoxyl in which the group $-AsO(OH)_2$ is attached to aniline; similarly the beginning of the bactericidal substances is sulphanilamide in which the group $-SO_2.NH_2$ is attached to the dye aniline. We may remember also that aniline, when acetylated to make acetanilide, is a powerful antipyretic. We see that Ehrlich's idea

that a drug, like a dyestuff, must have an affinity for cellular tissues was remarkably accurate. A useful drug is one which like some dyes will differentiate between some cells and others; thus the ideal bactericidal drug is one which has an affinity for the cells of the invading organism but none for that of the host. Aniline itself is highly toxic, that is to say, it has an affinity for the cells of the host as well as for that of the invading organism. By putting in a sulphonic acid group, $-SO_2.OH$, all toxicity and affinity are lost, but if the slightly acid sulphonamide group, $-SO_2.NH_2$, is introduced instead of the strongly acid sulphonic acid group, the product has the right degree of acidity and solubility to differentiate between the cells of the invading organism and those of the host.

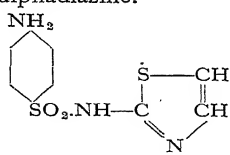
The Action of Sulphanilamide in Vitro.—Sulphanilamide has an action in vitro; when it is added to blood and this is infected with streptococci, the streptococci grow for the first two hours of incubation, and then rapidly diminish in numbers. If serum is used instead of blood the growth of the streptococci is arrested at the end of two hours, but the numbers do not then diminish; in the absence of the phagocytes the bacteria are not eaten up.

Comparison of the Sulphonamides

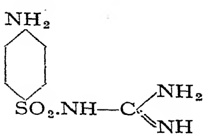
The principal sulphonamides in use to-day in addition to sulphanilamide are sulphapyridine (M. and B. 693), sulphathiazole, sulphanilguanidine and sulphadiazine.



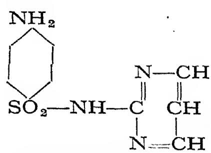
Sulphapyridine



Sulphathiazole



Sulphanilguanidine



Sulphadiazine

The solubilities of the different substances are given in Table XII, from which it appears that sulphanilamide is

TABLE XII

SOLUBILITY OF SULPHONAMIDE DERIVATIVES IN WATER AND URINE (pH 7·1) AT 37·5° C.

COMPOUND	SOLUBILITY IN WATER MG. PER 100 C.C.	SOLUBILITY IN URINE MG. PER 100 C.C.
Sulphanilamide	1480	—
Acetylsulphanilamide	534	—
Sulphanilguanidine	220	218
Acetylsulphanilguanidine	40	48
Sulphapyridine	54	57
Acetylsulphapyridine	16	19–34
Sulphathiazole	96	—
Acetylsulphathiazole	6	25–37
Sulphadiazine	12	—
Acetylsulphadiazine	15	85–88

much more soluble than the others, and that sulphapyridine, sulphathiazole and sulphadiazine all have a low solubility. In the body, when absorbed into the blood stream these substances are partly acetylated and so inactivated. This happens with sulphanilamide to the extent of 10–20 per cent. with sulphapyridine to 50 per cent. or more, with sulphathiazole to 25–30 per cent. and with sulphadiazine to 15–20 per cent. The acetylated forms, while inactive, have lower solubilities than the substance itself, and this lower solubility has been responsible for renal symptoms in patients treated with sulphapyridine and sulphathiazole. The acetyl derivatives of these substances are deposited sometimes as crystals in the renal tubules, causing lumbar pain and hæmaturia. This has never happened with sulphanilamide, and has not so far occurred with sulphadiazine, the acetyl derivative of which has a much higher solubility in urine than in water.

Thus it is evident that solubility affects the clinical use of the sulphonamide drugs. It might be thought to be the determining factor in absorption also. This, however, is not so. For sulphanilguanidine is more soluble than sulphapyridine or sulphathiazole, nevertheless the latter substances are absorbed

to greater extent. Some sulphanilguanidine is absorbed from the intestinal tract, but the greater part is not absorbed, and remains there to exert a bactericidal action which is of great value in dysentery and similar conditions. It is for disinfection of the intestinal tract that sulphanilguanidine is used.

Sulphapyridine (M. and B. 693) has been found to have a most valuable bacteriostatic action on the pneumoccus, against which organism sulphanilamide is ineffective. Sulphapyridine very often produces nausea and vomiting, and so far as it is available, sulphathiazole is replacing sulphapyridine because sulphathiazole is much better tolerated. Sulphathiazole is sometimes effective in the treatment of staphylococcal infections. Sulphathiazole is also recommended for the treatment of urinary infections, though its value for this purpose is difficult to understand because of its low solubility. Sulphadiazine promises to be a substance of great therapeutic value because a given concentration in the blood can be obtained with a smaller dose of this substance than with any other of the sulphonamides. While its solubility in water is low, its solubility in rabbit blood is as high as 247 mg. per 100 c.c.

Toxic Effects.—Toxic effects in addition to those mentioned are cyanosis, due chiefly to the formation of methæmoglobin which is often seen when sulphanilamide is administered; drug fever and skin rashes; anæmia and agranulocytosis. This last important symptom is not likely to occur unless the drug has been given for too long a time. Sulphanilamide treatment is generally confined to a period of 5–7 days during which large doses are given especially at first. If it is continued longer, it is important to look for changes in the blood picture. As a result of methæmoglobin formation, porphyrins are formed in the body and excreted in the urine; their presence in the blood may make the skin sensitive to light with resulting dermatitis.

Bacterial Infections of the Urinary Tract.—The treatment of acute infections of the urinary tract such as cystitis or pyelitis consists in the first place of giving fluids and alkalis. It is essential that the amount of fluid be specified; a man should take 8 pints of fluid in the day and sufficient sodium citrate to keep his urine alkaline. Citrates, acetates and tartrates are all oxidized to carbonate in the body and so

make the urine alkaline. This treatment is usually sufficient to reduce the temperature, to stop the frequency and pain of micturition and to render the urine free from pus. Sometimes the urine becomes sterile, but often it does not. After one week or 10 days of this treatment, infections due to *B. coli* are best treated with mandelic acid, though good results are occasionally obtained with hexamine. Hexamine, or hexamethylene tetramine, breaks down in an acid medium with liberation of formaldehyde. To administer hexamine the urine must therefore be made acid, for which purpose the patient takes sodium acid phosphate, in a dose of 2–4 gm. (30–60 gr.). The patient must discover the right amount, for too large a dose causes diarrhœa. Hexamine is then taken in a dose of 1 gm. (15 gr.) three or four times a day. In order to obtain the maximum concentration in the urine the intake of fluids is reduced to 2 pints. The urine must be tested at intervals for sterility.

Treatment with Mandelic Acid.—Treatment with mandelic acid originated with the observation that a high-fat diet sterilized the urine of patients with a urinary infection. On a high-fat diet the urine becomes very acid due to the excretion of β-hydroxybutyric acid, and this substance was found to be bactericidal. Many chronic infections with *B. coli* were cured by giving a high-fat diet. This diet is, however, unpleasant to take and not tolerated at all by some. A search was therefore made for other acids which could be given by mouth and which were excreted unchanged in the urine and which were bactericidal. Mandelic acid was found to be the most suitable.

The effectiveness of a given concentration of mandelic acid depends on the reaction of the urine; the more acid the urine the more bactericidal is mandelic acid. Accordingly it was first given together with ammonium chloride (1 gm. eight times a day) to make the urine as acid as pH 5·5, the fluid being restricted to 2 pints. At pH 5·5 the urine gives a reddish orange colour with methyl red. The dose of mandelic acid is 12 gm. a day, 3 gm. of mandelic acid being dissolved in 1 oz. of water and neutralized with 1·6 gm. sodium bicarbonate. The taking of 8 gm. of ammonium chloride is for many patients impossible owing to the nausea produced. The ammonium chloride may be cut down from 8 to 2 gm. or, instead, elixir of ammonium mandelate can be given.

Calcium mandelate is also efficient. If ammonium mandelate or calcium mandelate is given, no special steps are needed to make the urine acid, because it is believed that the ammonium or calcium mandelate is changed in the stomach into ammonium or calcium chloride and mandelic acid. The ammonium or calcium chloride reacts with the sodium bicarbonate in the intestine to liberate hydrochloric acid; thus $2NH_4Cl + NaHCO_3 = HCl + NaCl + (NH_4)_2CO_3$.

In the majority of patients an infection of the urine with *B. coli* is rapidly cured by mandelic acid. Infections with other organisms which resist mandelic acid treatment are treated with sulphanilamide or sulphathiazole.

CHAPTER XX

THE KIDNEY

Diuretic Substances.—Diuretics are substances which increase the flow of urine. There are three classes:

(*a*) substances which increase the non-colloidal constituents of plasma and therefore increase the amount of filtrate formed in the glomeruli of the kidneys; examples are water, sodium chloride and urea;
(*b*) purine derivatives such as caffeine, theobromine and theophylline;
(*c*) mercurial diuretics.

Water, Urea and Salts.—Urea is used as a diuretic in hydræmic or parenchymatous nephritis, when the kidney cannot excrete sodium chloride; in this disease the daily intake of sodium chloride must be reduced from the normal figure of 10 gm. to 3 gm. Urea is not reabsorbed in the tubules, and therefore when large amounts of urea are taken by mouth they are filtered off in the glomeruli and carry with them an amount of water corresponding to the osmotic pressure they exert.

Purine Derivatives.—In the ordinary working kidney some of the glomeruli are active and some are resting. When caffeine is administered there is a rise in the number of active glomeruli. Caffeine also causes a dilatation of the kidney vessels leading to increased blood pressure in the glomeruli and therefore to increased filtration. Some workers have produced evidence that caffeine lowers the osmotic pressure of the plasma proteins, and in this way also increases the effective filtration pressure. Diuretin is a preparation containing theobromine and sodium salicylate; it acts like caffeine.

Mercurial Diuretics.—The most important diuretics are the organic mercury compounds of which the best known is mersalyl (salyrgan is a proprietary name). Mersalyl is given together with ammonium chloride in order to make the reaction of the urine acid. The most probable explanation of the action of mersalyl is that like other compounds of mercury it has a toxic action on the tubules of the kidney and so prevents them from reabsorbing all the water which they reabsorb. In this way increased excretion of water is produced. Mersalyl is valuable in getting rid of œdema fluid, but it must not be used when there is any existing kidney disease.

CHAPTER XXI

LOCAL ANÆSTHETICS

The Action of Cocaine.—Cocaine is derived from the leaves of *Erythroxylon coca*, a plant growing in South America. The Peruvian Indians chew the leaves and can then perform feats of endurance. Cocaine is used in medicine as a local anæsthetic both for work on the eye and on the nose and throat, because in addition to paralysing the sensory nerve endings it causes dilatation of the pupil and vasoconstriction. Thus when cocaine is instilled into the conjunctival sac there is (*a*) local anæsthesia of the cornea and conjunctiva, (*b*) blanching of the conjunctiva so that operations can be carried out with little bleeding, (*c*) dilatation of the pupil and (*d*) widening of the palpebral fissure. The pupil when dilated by cocaine will still react to light, because the sphincter iridis is unaffected.

The dilatation is due to contraction of the dilator pupillæ. In contrast to this a pupil dilated with atropine will not react to light. Similarly the use of cocaine in work on the nose and throat is due to its power of causing local vasoconstriction which other local anæsthetics do not produce.

Toxic Effects of Cocaine.—Cocaine produces toxic effects which appear to be of two kinds. It produces convulsions and *it also produces collapse in which the respiration stops and* which is commonly believed to be due to failure of the respiratory centre. The convulsions when they occur can be controlled by the injection of a barbiturate, though care must be taken when injecting it, not to pass from convulsions to respiratory stoppage. The collapse due to respiratory failure is probably not central paralysis but rather peripheral failure of the impulses passing down the phrenic nerves to cross the neuromuscular junction to the diaphragm. That is to say the action of cocaine is curari-like. Persons in whom this collapse has occurred are sometimes conscious while artificial respiration is being applied; moreover, this form of collapse either with cocaine or procaine is readily produced in patients suffering from myasthenia gravis.

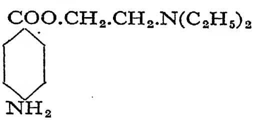
Cocaine as a Drug of Addiction.—Cocaine is well-known as a drug of addiction; the crystalline cocaine hydrochloride is sniffed up the nose, where it is rapidly absorbed through the nasal mucous membrane. Cocaine taken in this way produces cerebral excitement and intoxication.

Cocaine as a Sympathetic Stimulant.—Cocaine is a substance which in several respects resembles a sympathomimetic substance like ephedrine. Cocaine inhibits the rhythm of an isolated loop of intestine, and diminishes the tone of the isolated virgin cat's uterus; both these effects are adrenaline-like, or ephedrine-like. Cocaine dilates the pupil of the eye, and if the pupil is first denervated by removal of the superior cervical ganglion, the dilatation produced by an intravenous injection of cocaine is greater than in the normal eye, though cocaine has no effect when applied externally to an eye denervated in this way. On the blood vessels cocaine has a slight constrictor effect, but it has a striking effect in augmenting the constrictor action of adrenaline, which is due to the cocaine attaching itself to some of the molecules of enzyme which destroy adrenaline, so that the adrenaline is

destroyed more slowly than before. This ability of cocaine to attach itself to the enzyme is additional evidence that cocaine can attach itself to sympathetic receptors.

In muscle fatigue, the fatigue occurs principally at the myoneural junction, and the effect of this fatigue on the height of muscle contraction can be counteracted by sympathomimetic substances such as adrenaline or ephedrine. Cocaine also augments muscle contraction during fatigue, thus exerting the opposite effect in certain concentrations to that already described as a curari-like action. This augmentor effect is probably the basis of the use of coca leaves by the Peruvian Indians.

The Action of Procaine.—Procaine, also known as novocaine, is another local anæsthetic; it can be regarded as a derivative of aniline. Its formula is



Procaine is not a drug of addiction and is much less toxic than cocaine. In dentistry it is commonly used together with adrenaline; if procaine were injected alone, it would be carried away from the site of injection by the blood-stream, since procaine, unlike cocaine, does not constrict the blood vessels; the adrenaline constricts the vessels and thus prolongs the action of the procaine.

The low toxicity of procaine is due to the fact that it is absorbed slowly from subcutaneous tissues and destroyed by the liver as fast as it is absorbed. Despite this low toxicity symptoms sometimes follow the use of procaine, and collapse has been recorded in patients with myasthenia gravis; this collapse is due to an action on the motor nerve endings in skeletal muscle similar to that already described for cocaine. The paralysis of motor nerve endings produced by procaine is however much less than that produced by cocaine.

Solutions of procaine hydrochloride should not be sterilized by heat, but by passage through a bacteria-proof filter; they should be made up in normal saline. Procaine, like cocaine, augments the action of adrenaline by inhibiting one of the enzymes, amine oxidase, which destroy adrenaline.

The Action of Percaine.—For some purposes procaine appears to be too weak an anæsthetic to be reliable. Thus when used for tonsillectomy it is not always reliable, and when used for thyroidectomy so much has to be given that toxic effects follow. A much more potent anæsthetic is percaine or nupercaine. It is of course more toxic, but the increase in potency is greater than the increase in toxicity, and it is useful for tonsillectomy and thyroidectomy because so much less need be given, and its effect is reliable. Like procaine, it is given together with adrenaline. Instead of 2 per cent. procaine, 0·1 per cent. percaine is used.

CHAPTER XXII

SERUMS AND VACCINES

Diphtheria Prophylactic.—This term was introduced by the British Pharmacopœia to cover all those agents used in medicine for producing active immunity to diphtheria. Thus diphtheria antitoxin is *not* one of the forms of diphtheria prophylactic since diphtheria antitoxin, which is anti-diphtheritic serum or a derivative of it, is an agent used to confer passive immunity.

Diphtheria antitoxin is obtained from horses by giving them successive doses of diphtheria toxin until they form large amounts of diphtheria antitoxin in their blood. The diphtheria toxin is used in the horse as an immunizing agent; diphtheria prophylactic is a modified diphtheria toxin used in man for the same purpose. Thus diphtheria prophylactic is not a serum, but it is rather a vaccine, using this term to cover all agents used to provoke an immune reaction and to create active immunity. By a serum we mean (usually) horse serum containing an antibody such as diphtheria antitoxin; when the serum is injected into the patient a passive immunity is conferred.

The different forms of diphtheria prophylactic are (*a*) toxin-antitoxin mixtures, known as T.A.M., (*b*) toxoid, in which the toxin is rendered harmless by six months' treatment with formaldehyde, (*c*) toxoid-antitoxin mixtures, (*d*) toxoid-

antitoxin floccules, known as T.A.F., in which the neutralization of the toxoid by antitoxin is so exact that the mixture has formed macroscopic floccules, which are then centrifuged free from all other matter; (*e*) alum-precipitated toxoid (A.P.T.), in which the toxoid is precipitated by alum, and so when introduced into the body forms a small depot from which toxoid is slowly liberated into the circulation over a long period of time.

The great value of diphtheria prophylactic has not yet been recognized in this country. Diphtheria is the commonest single cause of death among school-children. In 1937 there were 61,339 cases of this disease in England and Wales causing 2,963 deaths, nearly all in children. Yet in those parts of the United States and of Canada where preventive inoculation has been universal, diphtheria has disappeared. In Hamilton, Ontario, with a population of 175,000, there has been no case of diphtheria in the last five years, although in the city of Quebec, where inoculation was not undertaken, the deaths are more numerous than ten years ago. In 1936 the death-rate of children from 1–15 years of age from diphtheria was 2·1 per 100,000 in New York, but was 31·8 per 100,000 in England and Wales.

Active Immunization.—In the immunization of animals it has been found that there are two stages. The first stage follows the injection of the first dose of diphtheria prophylactic or diphtheria toxin and consists of the production of a basal immunity. The first injection does not lead to the production of much antitoxin in the blood and what production there is is slow. The more important result of this first injection is to produce a condition in which the animal responds rapidly and abundantly to a second injection. Thus Glenny has observed that in guinea-pigs the first injection of diphtheria toxin produced an amount of antitoxin which on the average was 0·1 unit; there was a delay of 2–3 months in the appearance of this. After the second injection, the amount produced varied from 1–10 units, and appeared in 8–12 days. These results indicate that in immunizing children, it is probably best always to give two injections, and to allow 2–3 weeks between each injection. When A.P.T. is used, many people consider that one injection is enough, for as already explained, the toxoid is slowly liberated from the

store of precipitated material which is injected, and one injection is therefore equivalent to a continuous injection.

Diphtheria Antitoxin.—The use of diphtheria antitoxin for the treatment of diphtheria is so well-known that little need be said about it. Diphtheria antitoxin exists in several forms; the oldest form is the serum containing the antitoxin; the second form is a dry powder consisting of the dried serum; the third form is the precipitated globulins in the serum, to which the antitoxin is attached. The precipitated globulins can also be dried; this is the fourth form.

When diphtheria antitoxin is used in treatment, it is not generally realized that it is absorbed very slowly from the subcutaneous tissues, and slowly from the muscles. To obtain a rapid action it must be given intravenously. Diphtheria antitoxin stands in this respect in great contrast with ergometrine which is absorbed in the blood stream within a few minutes of being taken by mouth. Glenny gives the figures shown in Table XIII for the rate of rise of antitoxin in the blood expressed as a percentage of the amount found at the same time after intravenous injection. Six hours after intramuscular injection there is present only 11 per cent., and after subcutaneous injection there is present only 6·5 per cent.; even 24 hours later, the figures are about 50 per cent.

TABLE XIII

HOURS AFTER INJECTION.	ANTITOXIN CONTENT EXPRESSED AS A PERCENTAGE OF THAT PRESENT AT THE SAME TIME AFTER INTRAVENOUS INJECTION.	
	INTRAMUSCULAR.	SUBCUTANEOUS.
2	1·06	0·47
4	4·3	3·2
6	11·0	6·5
24	50·0	42·0
48	77·0	86·0
72	100·0	100·0

The Value of Different Serums.—The different antiserums vary much in their usefulness. There is good evi-

dence however for regarding the value of the following as established :

Diphtheria Antitoxin
Tetanus Antitoxin
Gas-gangrene Antitoxins, (*a*) perfringens
(*b*) vibrion septique
(*c*) œdematiens
Antidysentery serum (Shiga)
Antitoxins, (*a*) for certain snake venoms
(*b*) for scorpion stings
(*c*) for Botulinus
Convalescent measles serum
Scarlet-fever antitoxin
Anti-anthrax serum

Tetanus antitoxin is efficient as a prophylactic, though in the treatment of tetanus it is less satisfactory. Gas-gangrene antitoxins are also of value in the prophylaxis of grossly infected wounds, and in the treatment of gas-gangrene occurring with puerperal sepsis after abortion ; they can be used in abdominal surgery for the prophylaxis and treatment of the toxæmia of acute intestinal obstruction. Most information is available about the perfringens antitoxin, but the experience gained at the end of the war, especially by French workers, seems to establish the value of the vibrion septique and œdematiens antitoxins also.

Convalescent measles serum, applied at the proper time and in sufficient dose, is of value for measles. Unfortunately its potency cannot be measured and the dosage is therefore uncertain ; moreover the time at which it should be given to those who have been in contact with measles is sometimes not precisely known. Differences of opinion about scarlet-fever antitoxin exist. Those who have used it most are most convinced of its therapeutic value, especially in modifying symptoms, shortening the period of illness and in reducing complications and sequelæ. In some countries such as Roumania, Denmark and the United States convalescent scarlet-fever serum is used. In recent years convalescent human serum for the control of anterior poliomyelitis has been claimed to be of therapeutic value, especially in Denmark.

Authorities in Great Britain are less convinced of the efficacy of antibacterial serums in general, despite the evidence

from the United States of the high therapeutic efficiency of antipneumococcus serum of some types. In the United States many physicians consider that when the infecting type has been determined and the serum is available, it should always be given.

The efficacy of anti-meningococcus serum is doubtful. Very little information is yet available of the treatment of human beings with staphyloccus antitoxin; it should be of value in controlling staphylococcus toxæmia at least, and experiments on animals suggest that it should be of value in the treatment of certain kinds of staphylococcus infections.

There is no evidence to show that anti-plague serum or anti-cholera serum are of therapeutic value, but there is good evidence for the use of antidysentery serum (Shiga) and for anti-anthrax serum.

SECTION II

PHARMACY

CHAPTER I

THE COMPOUNDING AND DISPENSING OF PRESCRIPTIONS

The term " Compounding " applies to the mixing, blending and preparing of the drugs ordered in a prescription, while " Dispensing " refers to the way in which they are put up, labelled, and sent out to the patient; thus the incorporation of a mixture of several substances is spoken of as its " compounding," after which it is to be " dispensed " in a flat, square or round bottle; but if a prescription, for example, should contain an order for twelve 5-grain Dover's powders, it would be simply a case of dispensing, since the medicine is always kept compounded by the dispenser.

The practitioners of former days were in the habit of saying that " no one should be allowed to *write* a prescription unless he is able to *compound* it," and if such were the rule of Examining Boards, doubtless more useful and more elegant prescriptions would be the fashion; and even if the above adage were not true, the training requisite to make a good dispenser would be a great accomplishment to the practical physician, teaching him habits of neatness, readiness and accuracy, and giving him a practical acquaintance with drugs obtainable in no other way.

The compounding of medicines can only be really learned at the dispensing counter; but a few general directions will be here given as a guide to the student. It is an essentially

practical study; once the prescription is in the hand of the dispenser he must give to it his undivided and concentrated attention. Day-dreaming must be for the moment laid aside, and in proportion to the thoroughness with which he isolates himself from everything but the sheet of paper before him, so will his success be. The carrying on of a conversation whilst dispensing is a very dangerous practice, and should be discouraged.

Dispensing should be governed by the following: *Accuracy*, *Cleanliness*, and *Speed*, and the student must train himself to a rigid routine. Accuracy and cleanliness should be cultivated first, speed will follow later.

The **Prescription** should be clipped up in front of the dispenser in order to minimize the risk of soiling it during dispensing. It should be read carefully through, and any unusual dose or incompatibility noted. The dispenser should realize that the Pharmacopœia lays the onus of the responsibility of dispensing an overdose on him by the paragraph contained in the General Notices, p. 5, which states that "The medical practitioner will exercise his own judgment and act on his own responsibility in respect of the amount of any therapeutic agent he may prescribe or administer. When, however, an unusually large dose appears to have been prescribed, *it shall be the duty of the pharmacist or dispenser* to satisfy himself that the prescriber's intention has been correctly interpreted."

When the dispenser feels that he cannot accept the responsibility of the prescribed dose, he should get into touch with the prescriber and have the amount confirmed, and, if possible, initialled. Most prescribers will usually initial any unusual dose, and thus inform the dispenser that such is intentional. The prescriber should be also consulted if an incompatible is discovered which, in the dispenser's opinion, is dangerous or which prevents the intention of the prescriber from being carried out. Difficulties in reading and deciphering may be experienced, but they will nearly always disappear on a careful comparison of the formation of the letters in the doubtful word with those in the unmistakable portions of the prescription.

The **Label** should be written in ink before commencing dispensing, and allowed to dry without blotting. By

writing it before the operation the mind is switched away from it to the actual dispensing, and finally returns to it for a second checking when it has to be placed on the bottle or package. In this way it is often possible to discover a mistake in directions, which might otherwise be passed.

Weighing.—The essential feature here is accuracy, with speed as a secondary but important consideration. Two types of balances will be found in a dispensary: (*a*) The ordinary fixed upright beam and scales which are provided with one movable glass pan which should be opposite the dispenser's right hand and on to which the substance to be weighed is to be gradually placed, the weights having been previously put on the opposite pan. This type of balance is intended for quantities ranging from 1 grain to 1 ounce (Fig. 10); (*b*) a fine balance of the type used in a chemical laboratory for analytical work. On this should be weighed all potent substances (i.e. substances with a maximum dose of 1 grain or less). Students will notice this difference that, whilst in the chemical laboratory they were accustomed to putting the substance to be weighed on the *left*-hand side, in dispensing it is put on the *right*-hand side. A little consideration will determine the reason for this apparent difference. The right-hand pan is the one which is manipulated: in chemistry the weights are adjusted to the substance, whilst in dispensing the substance is adjusted to the weights, and unless the operator is left-handed, the more convenient side for making adjustments is the right side.

In the Apothecary system the smallest weight usually supplied is $\frac{1}{2}$ grain (0·03 gramme), but in the metric system the smallest weight is 1 milligramme (0·001 gramme). When dealing with a very small quantity, say about 1 milligramme, it is easier to adjust the weights to it than to adjust the substance to a very small weight. The student should appreciate the importance of being very accurate in weighing when dealing with a toxic substance such as Atropine Sulphate, the *maximum* dose of which is $\frac{1}{60}$ grain or 0·001 gramme. For this reason the following rule is generally adopted: "Never weigh less than 1 grain or 0;05 gramme, and always weigh it (particularly if a toxic substance) on the fine balance." Fractions of a grain can be obtained by making a solution or trituration (see p. 180). In the ordinary routine of dispensing, the dispenser will rarely want more than 1 grain of the type

of toxic substances mentioned, and should his calculation require more, it should be most carefully rechecked.

Other routine precautions in weighing are :—

Check the accuracy of the balance by giving it a trial swing

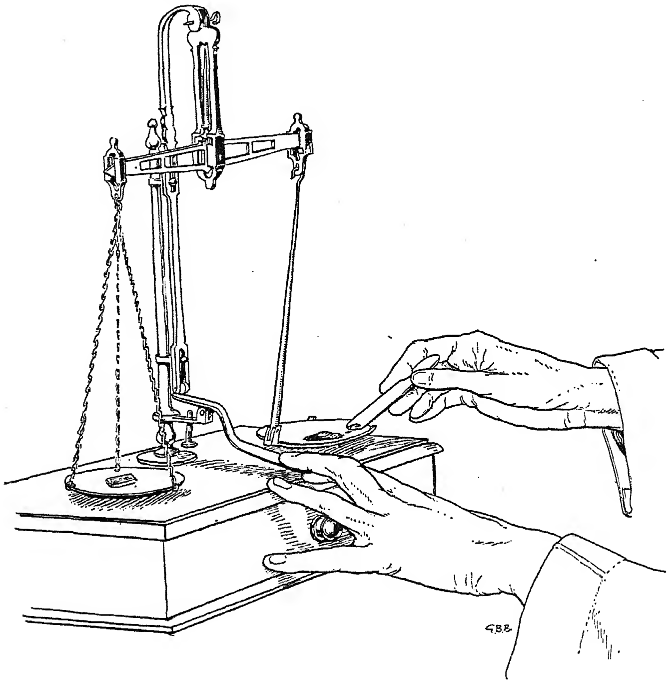


FIG. 10.

before commencing dispensing. It may be out of adjustment or sticking.

Always wipe the pan immediately after each weighing. Neglect of this precaution generally means the contamination of most of the drugs in the other bottles.

Keep the scale drawer closed, otherwise it soon accumulates a collection of materia medica, as well as weights, which latter quickly become inaccurate.

Never tap the glass pan on the sides of the mortar when shaking off the contents. It chips and becomes inaccurate.

Weigh sticky extracts or similar substances on a small piece of parchment paper, counterbalancing with a similar piece.

Never have more than one bottle of an ingredient on the dispensing counter at the same time, and always replace immediately after use. Neglect of this can cause serious trouble by facilitating the accident of weighing two quantities of the same ingredient and excluding another.

The **Measuring** of liquids is a simple process, but, like many others, requires care and practice, and should be done always according to rule. All measures, except the

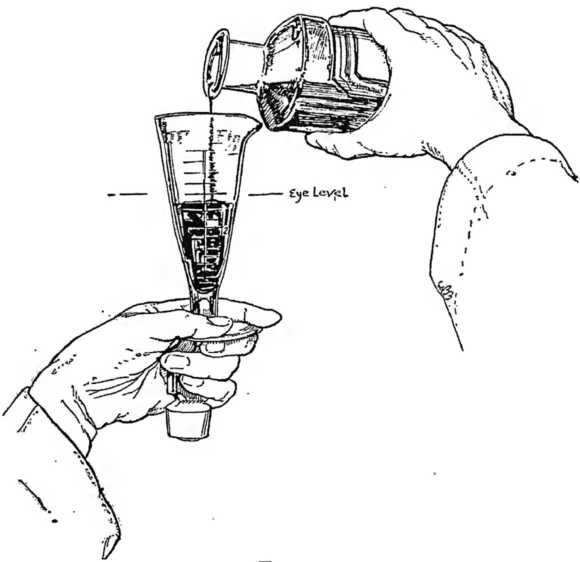


FIG. 11.

heavy ones, should be held *perfectly upright* between the thumb and next two fingers of the left hand (Fig. 11) and raised to the *level of the dispenser's eye*. The bottle is grasped firmly by the right hand, the stopper being previously withdrawn and held by the little finger of the opposite hand. The liquid is then poured out, the uprightness of the measure being

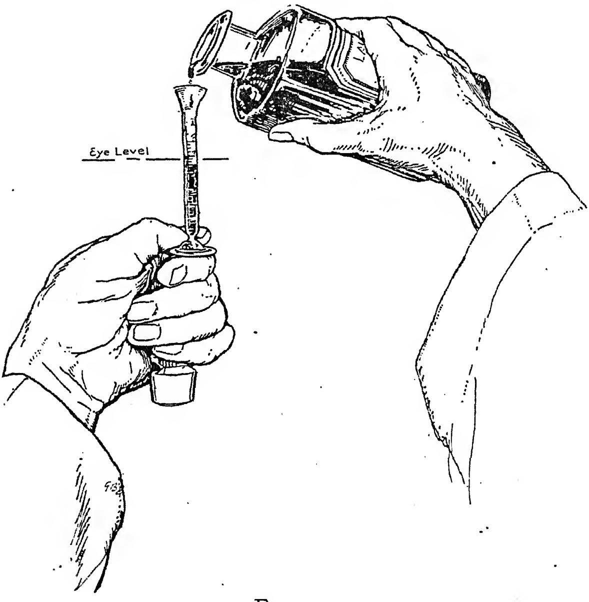


FIG. 12.

verified by making the lines on the front and back of the measure coincide. As in the reading of a pipette or burette, the bottom of the meniscus is taken as the true measuring line. Always grip the bottle so that the label is upwards (as in Fig. 12), so that any drop of liquid left on the lip will not trickle down over it and make it unsightly.

Always choose a suitable sized measure for the particular

quantity required, and do not attempt to measure ʒi. in a ℥iv. measure.

Never measure one liquid on top of another, and after measuring a thick liquid, like glycerin, always rinse it out before measuring another liquid, otherwise an inaccuracy will occur due to the lining of glycerin.

The student should appreciate the difference in accuracy between the conical measure with its *wide* meniscus and the cylindrical one with its *narrow* meniscus.

An error made in reading the level of the liquid results in a much larger excess or deficiency in the conical one than in the cylindrical one. Conical measures, on the other hand, are easier to clean and, being squat, have a greater stability than the tall cylinder.

For the measurement of small quantities, it is advisable to use the type of measure as in Fig. 12, which, too, is generally held as depicted, so that the thumb does not interfere with a reading. When quantities of 10 mins. or less are required, particularly if the liquid is very volatile, such as hydrocyanic acid, it is advisable to use a graduated pipette fitted with an india-rubber bulb (like a fountain-pen filler).

The minim and the drop are not synonymous, as the size of a drop will vary with different liquids and with the type of container from which it falls. For this reason it is better to use a graduated minim pipette.

Checking.—It is always advisable that all quantities of potent substances or their preparations—whether weighed or measured—should be checked by a second person before being incorporated in the preparation. For the purpose of this rule, a potent substance might be defined as one having 1 grain or less as a maximum dose.

The Pestle and Mortar.—A good selection of mortars is essential on the dispensing counter, and the student will find that there is much to learn in choosing the right type and using it in the correct manner for the particular operation. There are three main types:

(*a*) *The glass mortar*, usually small and used for very light grinding and trituration, particularly when dealing with very small quantities of toxic substances. It is very suitable when Iodine has to be rubbed down, as it is not stained.

(*b*) *The metal mortar*, made of iron, brass, or bell metal, and used when heavy contusion or crushing is required which would break other more fragile types.

(*c*) *The porcelain, composition or wedgwood mortar*, made of earthenware and varying very much in quality. The best type is the smooth, glazed wedgwood mortar, which does not stain as readily as the rougher, cheaper variety. The wedgwood mortar is the type for general use in grinding, levigating, mixing, pounding, etc.

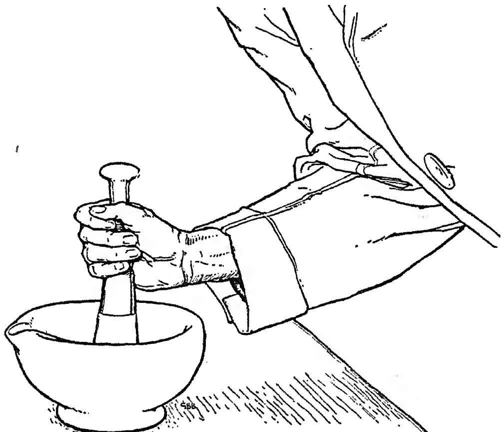


FIG. 13.

The shape of the pestle is an important consideration, for it may have a rounded base or a flattened base. The latter is the better type, as it provides a good shearing surface and is more suitable for grinding and levigating than the former. For the proper levigation of ointments and the preparation of emulsions it is essential to have a good, well-fitting, flat-headed pestle. It is important to realize that there are four distinct methods of *holding* and swinging the pestle according to the particular operation, and the student must appreciate them.

1. As in Fig. 13, where the pestle is firmly grasped about

one-third of the way down by the right hand and power is applied from the shoulder and arm, the wrist being kept rigid and the elbow nearly stiff. By a series of rotatory movements in an *anticlockwise* manner, chiefly at the shoulder-joint, the pestle is made to travel *slowly* round the interior of the mortar in ever gradual increasing and then decreasing orbits, so that the whole of the interior is covered.

This is the grinding and levigation action when a fair amount of power is necessary.

2. As in Fig. 14, where the pestle is lightly grasped in the same manner as a pen is held and a swift, graceful movement is communicated by the *wrist* and with no motion at the elbow or shoulder.

FIG. 14.

This is the mixing or triturating action when a quick action with little pressure is required.

3. As in Fig. 15, when the end of the pestle is placed in the palm of the right hand and firmly grasped whilst the left hand grips a shallow mortar. The pestle is used as a lever, with the edge of the mortar next the dispenser as a fulcrum, and great force is necessarily applied in order to squeeze slowly the substance between the end of the pestle and the side of the mortar at each slow stroke. The mortar is turned round occasionally so that all parts of the material or mass is exposed to the action of the pestle.

This is the massing or kneading action used in the preparation of pill masses.

4. Grasping the pestle as in Fig. 13 for grinding, but the

forearm is raised and lowered alternately—as a gold-beater uses his mallet—all the motion being confined to the elbow-joint.

This is the pounding or contusing action for use with a metal mortar, or more carefully with a wedgwood one, when it is required to reduce large lumps to smaller ones prior to finer grinding.

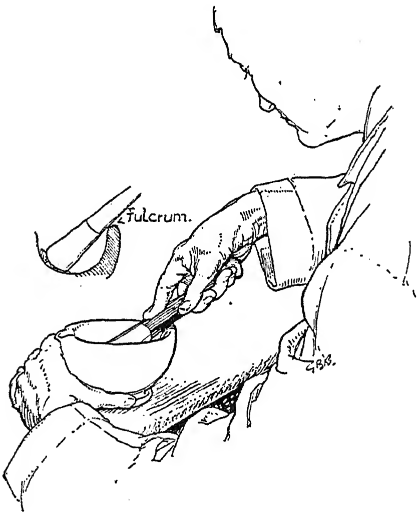


FIG. 15.

The student will do well to reflect upon these different methods of using the mortar and pestle, as required for different results, for this will teach him more than a year's blind practice. Unless he has some idea of the correct action of the machine, he can scarcely chance to wield the pestle efficiently or gracefully.

CHAPTER II

MIXTURES AND SIMILAR PREPARATIONS

This class of preparation contains a very wide and varied collection of types, and may consist of simple solutions, suspensions or emulsions. It would be difficult to give such general directions to the dispenser as would equally apply to the preparation of so many really different compounds, but a little practical experience will soon show him how he may apply the knowledge gained in making one class of preparation to aid him in compounding another. The dispenser should always bear in mind that, in manipulation of the preparation, he must preserve the full and correct therapeutic value of the ingredients and at the same time blend them together in as palatable a manner as possible, and in a condition which permits of an accurate dose being measured.

Mixtures are prescribed and dispensed in 2, 3, 4, 6, 8, 10 and 12 ounce bottles, and occasionally in 16 and 20 ounce. It is customary, in many dispensaries, for the bottles to be tested for accurate capacity before being placed on the shelf at the disposal of the dispenser. Inaccurate ones are rejected. If this plan be adopted, the mixture may be made up to volume in the bottle and not in a measure. The bottles should be of good quality white flint and *ungraduated*, as the graduations are usually quite inaccurate. The patient should be encouraged to measure the doses in a graduated medicine glass, and should a large dose of a potent substance be prescribed, the dispenser would be well advised to write on the label, "Take one *measured* tablespoonful" instead of "Take one tablespoonful." The average domestic tablespoon is not an accurate measure.

The label should be neatly written in ink, headed "The Mixture," followed by the directions, with the patient's name at the right-hand bottom corner.

If it is necessary to shake the preparation before measuring a dose, a "Shake the Bottle" label should be placed on the shoulder of the bottle just above the label. When any doubt arises as to the necessity for such a label it should always be put on.

Good quality *corks* only should be used, and they should be of the correct size, firmly fitting when inserted one-third of their length into the neck of the bottle.

The *vehicle* or solvent of the mixture may be distilled water, an aromatic water like peppermint water or chloroform water, or an infusion or decoction.

It is quite impossible to discuss every variety of mixture, but the following are representative types :

A. When all Ingredients are Soluble.

Consider the following prescription :—

1. ℞.

Boracis gr. iii.
Potass. Bromid. gr. v.
Sodii Bromid. gr. v.
Ammon. Bromid. gr. v.
Aq. chlorof. *ad* ℥ss.

Ft. mist. *Mitte* ℥vi. *Sig.* ℥ss. *s.o.s. sumendum.*

Since the quantities given in the prescription are for half a fluid ounce of mixture and six fluid ounces are required, the final quantities to be dispensed are :—

Borax . . .	$3 \times 12 = 36$ gr.
Potassium bromide	$5 \times 12 = 60$ gr.
Sodium bromide .	$5 \times 12 = 60$ gr.
Ammonium bromide	$5 \times 12 = 60$ gr.

The above salts are all soluble in water, hence weigh out the correct quantities and dissolve in the vehicle either with the aid of a pestle and mortar or by stirring in a measure. Add the vehicle in reasonably small quantities and pour off each quantity through washed animal wool into the bottle. Finally when all the salts have dissolved, swill out the measure or mortar with a little vehicle and wash through the animal wool. Then make up to volume in the previously graduated bottle (see page 163).

NOTE.—(*a*) Animal wool is a useful material for straining solutions and is recommended in preference to cotton wool, since the length of the fibre is longer and consequently there is less likelihood of small fibres being washed through into the bottle.

(*b*) The vehicle is chloroform water. This is usually stocked as a double strength solution, hence three fluid ounces will be used in this preparation.

2. ℞.

Ferri et Ammon. Citratis ʒiii.
Liquoris Arsenici ʒi.
Syrupi ℥i.
Aq. chlorof. ad ℥vi.

Misce. Ft. mist. Sig. ℥ss. *t.d.s.*

Here the quantities prescribed are sufficient for six fluid ounces. The iron and ammonium citrate is an example of a class of compounds known as scale preparations. The scales are readily soluble in water, but require careful treatment as they form sticky masses which are difficult to manipulate. Further the solution froths very readily. To avoid these troubles place the scales on the surface of the vehicle in a measure and dissolve by gently stirring. Proceed as for mixture (1) until all the citrate is dissolved. Add the syrup and lastly the arsenic solution and make up to volume. Remember that less than three ounces of double strength chloroform water is required since the syrup and solution together take up nine drachms. Assuming also that the solid citrate occupies half its weight in volume (i.e. one and a half fluid drachms), the quantity of double strength chloroform water required is

$$\frac{6 \text{ fluid ounces} - (1 \text{ fluid ounce} + 1 \text{ fluid drachm} + 1\tfrac{1}{2} \text{ fluid drachms})}{2}$$

$= 18\frac{3}{4}$ fluid drachms,

which can be taken as 19 fluid drachms.

NOTE.—(*a*) A persistent froth in the bottle is very troublesome when adjusting to volume. It can be avoided in this case if care is taken not to shake the mixture before making up to volume. Froth can easily be dispersed, however, by the addition of a few drops of alcohol.

3. ℞.

Sodii Salicylatis gr. x.
Sodii Bicarbonatis gr. x.
Potassii Citratis gr. x.
Inf. Gent. Co. ad ℥ss.

Ft. mist. Mitte ℥viii. *Sig.* ℥ss. *t.d.s.p.c.*

Similar considerations apply to this mixture as to mixture (1) save that the sodium bicarbonate is not readily soluble in water. It requires to be triturated in a mortar with successive quantities of the vehicle until dissolved.

NOTE.—(*a*) In the dispensing of this prescription concentrated compound infusion of gentian (Inf. Gent. Co. Conc. B.P.) can be used. Remember it is eight times as strong as the fresh infusion and therefore a little less than one fluid ounce of the concentrated infusion is required for the eight ounces of finished mixture.

Mixtures 1, 2 and 3 contain substances all of which are soluble in water. Here are a few more points that have to be remembered.

(i) If the substance is soluble in the amount of water prescribed, but the rate of solution is slow, hot water may be used to facilitate solution. Always providing, of course, that the hot water does not decompose any of the ingredients. Thus hot water should not be used to dissolve sodium bicarbonate since decomposition occurs with formation of carbonate and liberation of carbon dioxide.

(ii) Sometimes the ingredient is ordered in excess of its solubility. It must be finely powdered and dispensed with cold vehicle. The use of hot vehicle is inadmissable for although a solution might be obtained, subsequent cooling would cause the separation of the solid in crystalline form.

(iii) Liquids containing volatile constituents should be added to the bottle immediately prior to adjustment to volume. They should never be poured into a mortar or exposed for any length of time in an open measure. Here are some typical liquids of this type :—

Dilute solution of hydrocyanic acid (Acid. Hydrocyan. Dil. B.P.).
Aromatic spirit of ammonia (Spirit. Ammon. Aromat. B.P.).
Æthereal spirit of nitre (Spirit. Æther. Nitrosi B.P.).

B. When Insoluble Ingredients are Present.

4. ℞.

Bismuth. Carb. gr. v.
Sodii Bicarb. gr. xv.
Mag. Carb. Lev. gr. x.
Aq. Menth. Pip *ad* ℥ss.

Ft. mist. *Mitte* ℥vi. *Sig.* ℥ss. *t.d.s.a.c.*

The bismuth and magnesium carbonates are insoluble in water. The question is then, whether it is sufficient to mix them by simple trituration with water and dispense in suspension. Does this method yield a mixture from which the patient, after shaking the bottle, can measure a tablespoonful

containing the correct amount of solids ? With the solids here prescribed, the answer is " yes." Therefore mix the powders in a mortar and make into a smooth paste by gradual addition of water. Transfer to the bottle with the help of a funnel, add the correct amount of concentrated peppermint water and adjust to volume.

5. ℞.

Acid. Acetylsalicyl. ʒiv.
Phenacetin. ʒi.
Caffeinæ ʒss.
Aq. ad ℥viii.

Ft. mist. Sig. ℥ss. *dum cephalagia urgeat.*

Here the aspirin and phenacetin are insoluble and moreover require suspending. That is, to ensure correct and even dosage, the dispenser must add some inert substance which will keep the powders evenly distributed throughout the mixture whilst a dose is being poured out. Mucilage of tragacanth is quite efficient for this purpose. The quantity to use is not more than one fluid drachm to each fluid ounce of finished mixture. To prepare the above preparation finely powder the three substances in a mortar. Add to them the mucilage of tragacanth and then gradually add the water until a smooth cream results. Transfer to the bottle and make up to volume. Attach " Shake the bottle " label to the bottle (see p. 163).

NOTE.—Compound powder of tragacanth (Pulv. Trag. Co. B.P.) can be used and is very satisfactory for suspending insoluble powders. It is used in quantities of from 5–10 gr. per fluid ounce of finished mixture. A smooth cream is made by mixing the finely powdered insoluble substance with the suspending powder and adding water gradually. The compound powder of tragacanth is a mixture of tragacanth, acacia, starch and sucrose all finely powdered. It is much easier to make an elegant smooth preparation using this mixture than using powdered tragacanth alone. Recent work has purported to show that when acacia and tragacanth are both present, the viscosity of the finished preparation is less than that of one made with either of these gums used separately. Further, the use of the sucrose has been questioned. In spite of all these criticisms, compound powder of tragacanth is a very useful suspending agent.

Here is a list of substances which require suspension and for which either mucilage of tragacanth or compound powder of tragacanth could be used.

Acetanilide	Guaiacum resin
Acetylsalicylic acid	Methyl sulphonal
Barbitone	Phenacetin
Benzoic acid	Quinine salicylate
Bismuth salicylate	Salol
Guaiacol carbonate	Sulphonal

An example of the use of compound powder of tragacanth in a mixture official in the National Formulary is

Mist. Cret. Aromat. c̄ Opio.

6. ℞.

Pulv. Creta. Aromat. gr. xx.
Pulv. Trag. Co. gr. v.
Tinct. Catechu m. x.
Tinct. Opii m. v.
Aq. chlorof. ad ℥ss.

7. ℞.

Tinct. Asafœtidæ ʒiii.
Potassii Bromid. ʒiii.
Aq. ad ℥vi.

Ft. mist. Sig. ℥ss. *b.i.d. sumendum.*

This mixture contains a resinous tincture, that is Tincture Asafœtida is a solution of resin and oil in alcohol. Since resins are insoluble in water, the addition of this tincture to the water results in an unsightly precipitate. The more so because in this case potassium bromide is present and being dissociated in solution will coagulate any fine particles of resin that are formed by the change of solvent. Thus clots of resin are formed which stick to the sides of the bottle and render correct dosage impossible. The principle adopted in dealing with this difficulty is to make use of mucilage of acacia as a protective colloid. By this is meant the power of the acacia in preventing the coalescence of the asafœtida resin particles into large clots. Mucilage of acacia may be used in quantities of a half to one fluid drachm per fluid ounce of mixture. In this case mix six drachms of mucilage of acacia with twice that quantity of water and place in the bottle. Shake gently so that the whole of the surface of the bottle is covered with mucilage. Then pour the tincture into the bottle a little at a time and in a thin stream, shaking between each addition. Dissolve the bromide in the maximum quantity of water per-

missible and add to the resin suspension and adjust to volume. Affix a "Shake the bottle" label. Many other preparations behave in a similar way when mixed with water:

Ammoniated tincture of guaiacum
Ammoniated solution of quinine
Compound tincture of benzoin
Liquid extract of hydrastis
Tincture of Indian hemp
Tincture of myrrh
Tincture of podophyllum
Tincture of tolu.

A good example of the action of electrolytes in coagulating a resinous suspension is the following:

Tincture of myrrh if carefully diluted with water yields a light yellow colloidal suspension of resin which can be preserved for some time before coagulation occurs. If a fair quantity of electrolyte is present, however, say potassium chlorate or alum, then the tincture must be treated as with Asafœtida; in other words, without an electrolyte Tincture of Myrrh needs no protective colloid, with an electrolyte mucilage of acacia is indicated.

C. Miscellaneous Mixtures.

1. ℞.

Acid. Acetylsal. gr. viiss.
Potassii Citrat. gr. xv.
Aq. chlorof. *ad* ℥ss.

Ft. mist. *Mitte* ℥x. *Sig.* ℥ss. *s.o.s.*

Aspirin, whilst insoluble in water, dissolves in alkali citrates and acetates. The reaction is facilitated by warm water.

2. ℞.

Paraldehyd. ʒiss.
Aq. *ad* ℥i.

Ft. mist. *Mitte* ℥iv. *Sig.* ℥i. *h.s.s.*

This is an example of a slightly soluble liquid in a mixture. A distributive agent that will keep the globules from coalescing is necessary and mucilage of tragacanth serves very well. Place half an ounce of the mucilage in the bottle, dilute with

an equal quantity of water, add the paraldehyde and shake well. Adjust to volume. Affix a "Shake the bottle" label. Other sparingly soluble liquids are creosote and amyl nitrite. It must be remembered however that in the presence of alcohol these liquids may be more soluble. If in small doses (creosote) they may even be entirely soluble. So that if a tincture is included in a mixture, dissolve the creosote in it and add the solution gradually to half of the vehicle with continual shaking.

3. When a prescriber orders a carbonate to be dispensed with an acid, the intention is that the mixture shall be saturated with carbon dioxide. Thus the reaction must take place in a measure before bottling and furthermore must be completely finished before any attempt is made to cork the bottle.

Another point is that hot water should not be used to hasten the reaction, since this would result in more carbon dioxide being lost than is warranted.

Draughts (Haustus) are mixtures which contain only one or two doses. Their preparation differs in no way from an ordinary mixture.

EXAMPLE.—Haustus Chloral. N.F.

Chloral. Hydrat. gr. xx.
Potass. Brom. gr. xxx.
Ext. Hyosc. Liq. m. v.
Syrup. ʒii.
Aq. ad ℥iss.

Elixirs.—Elixir is the name given to a special type of mixture which contains considerable quantities of alcohol and often aromatic ingredients such as volatile oils. They are well sweetened and used as a vehicle for potent and nauseous drugs. The finished product should be bright and clear, and if it is cloudy, due to excess volatile oil, this excess can be removed by shaking with talc or kaolin and filtering. Elixirs should be well diluted at the time of administration. Many examples will be found in the B.P.C. under the title Elixiria.

Linctuses (Lincti).—A linctus is a mixture containing medicaments which have an action on the membrane of the throat and possess demulcent, expectorant or sedative properties. They contain much mucilage or syrup, and should be

directed to be sipped and swallowed slowly without the addition of water.

Drops (Guttæ).—Certain galenicals like tincture of digitalis, tincture of Strophanthus and liquid extract of ergot, lose activity rapidly if diluted with water, consequently they are prescribed *per se*, without dilution, and the patient is directed to take a definite number of drops. To facilitate administration dilution of these drops is advised prior to swallowing the dose. With each prescription dispensed a minim dropper or minim measure should be included.

CHAPTER III

EMULSIONS

An emulsion is a mixture of two liquids which are insoluble in each other, one of which being finely divided and dispersed in the other and prevented from coalescing again by the presence of a third substance, the emulsifying agent or emulgent. Thus oil and water can form an emulsion which, if a suitable emulgent is present, may be rendered permanent. With some emulgents (such as mucilages of gums, saponin, yolk of egg, hard, soft and animal soaps) the oil will disperse in the water, forming what are known as oil-in-water emulsions, whilst other emulgents (such as wool fat, wax, resin, calcium oleate or stearate) will cause the water to disperse in the oil, forming water-in-oil emulsions. Many ointments and liniments are of this latter type, such as hydrous ointment. The type that we are chiefly concerned with here is, however, of the oil-in-water type, and only such will be subsequently described in this chapter. Such an emulsion provides a very good method of administering certain fixed or volatile oils, and oleo-resins, which by themselves being nauseous and unpalatable, can be made palatable and miscible with water by being finely divided and dispersed in some aqueous vehicle which is generally sweetened and flavoured.

The nauseous taste is not noticed as only the continuous phase, the flavoured vehicle, is detected by the palate.

Acacia Emulsions.—For the preparation of oil-in-water emulsions for internal use, such as cod-liver, castor, and olive oils, acacia gum is probably the most favoured emulgent. It is generally used in fine powder, and in the following proportions :

(*a*) For fixed oils, such as the above, a quarter the quantity of gum as oil. Thus ℥i. of oil would require ʒii. of powdered gum.

(*b*) For volatile oils, such as turpentine, half the quantity of gum as oil.

(*c*) For oleo-resins, such as Copaiba, Extract of Male Fern, equal quantities of gum and oil.

If, however, the proportion of oil is less than about 20 per cent. of the final mixture, it will be found necessary to increase the quantity of gum to prevent creaming at the top on standing. Powdered Tragacanth is often added to Acacia emulsions for this purpose.

A good, smooth wedgwood mortar should be used with a *flat-headed* pestle. The oil should be measured and allowed to drain thoroughly into the mortar. The powdered gum should now be added, and *quickly* mixed with the oil, a measured quantity of water added, and the whole lightly and briskly triturated, holding the pestle as in Fig. 14, swinging it in circles that tend to cover every portion of the inner surface of the mortar. It is very important that (*a*) the oil and gum should not be left in contact longer than necessary before adding the water (this is a frequent cause of failure) ; (*b*) that the pestle should not be swung on one track only, but should tend to cover the whole of the inner surface of the mortar. The quantity of water added should be always *twice as much as gum used.*

If the procedure is correctly carried out, a very thick white emulsion will form (called the primary emulsion) which will crackle with the pestle. The pestle and the upper parts of the mortar should then be carefully scraped with a spatula and the scrapings added to the rest of the emulsion and thoroughly incorporated. It will pay the student to spend some time on the primary emulsion, as on it depends the success of the preparation. If the primary emulsion is properly made, the final emulsion will not go

wrong, and *vice versa* if it is badly made, the final emulsion will be a poor one. When satisfied that the primary emulsion is correct, it may be gradually diluted with portions of the vehicle and made up to volume. Strong alcoholic ingredients should always be diluted before adding them to an emulsion, and salts should be dissolved in the vehicle and diluted as much as possible before incorporating.

Acacia emulsions keep well and do not require the addition of a preservative.

Yolk of Egg Emulsions.—The yolk of an egg has twice the emulsifying power of acacia, and is used for emulsifying oils such as cod liver and olive because of its nutritive value, and also for certain liniments such as those containing acetic acid, in which soap could not be used. Yolk of egg emulsions are easily prepared. The yolk is separated from the white, placed in a good emulsion mortar, and rubbed quite smooth with the pestle. It is an advantage to incorporate about 2 gr. of powdered tragacanth. The oil is measured, a small quantity added to the yolk and incorporated, then a small quantity of the vehicle, and thus alternately oil and vehicle is added until all the oil is incorporated. Any other ingredients are then added and the emulsion adjusted to volume with the vehicle. Yolk of egg is a good emulgent, but it usually requires some preservative if the preparation has to keep for some time. Benzoic acid or sodium benzoate is generally used for this purpose.

Saponin Emulsions.—Saponin is a mixture of glycosides contained in such drugs as Quillaia and Senega, and has the property of causing water to froth very considerably when shaken with it. A solution of it will emulsify oils, but such emulsions tend to cream and look unsightly. Moreover, it has a therapeutic action of its own, and unless specifically prescribed should not be chosen by the dispenser. It is generally used in the form of Tincture of Quillaia, usually for emulsifying such substances as Extract of Male Fern, Balsam of Copaiba, and chloroform. The emulsions are easily prepared, the medicament being measured and the Tincture of Quillaia being poured on top in the same measure. They are well mixed with a glass rod, poured into the bottle, about twice their volume of water added, the bottle corked and well shaken. The aqueous vehicle is then added to volume.

Casein Emulsions.—Casein, which is obtained from milk, is used as an emulgent, usually in the form of soluble casein. The latter is obtained by the action of alkali on casein.

The soluble casein is mixed with the oil in a mortar and the aqueous vehicle is then gradually incorporated.

Casein emulsions do not keep, and require a preservative.

Irish Moss Emulsions.—A mucilage is prepared from Irish moss, by first washing with cold water and then digesting it with hot water on a water-bath, straining and cooling. The oil is gradually incorporated in the mucilage with constant trituration. Irish moss emulsions do not keep, and require a preservative. It is not often employed for the production of small quantities of emulsions, but is extensively used on a large manufacturing scale.

Small Emulsion Machines.—A number of inexpensive and efficient emulsifying machines can now be obtained. Good models are the "Empire" and "Pentecreme" types. These machines render the somewhat difficult technique of preparing a good "hand made" emulsion almost unnecessary. It is sufficient to prepare a roughly made emulsion and then pass it through the machine (this takes a very short while). The first runnings are generally returned to the reservoir and put through again. In the Empire model there is a milled-headed nut which can be adjusted to increase or decrease the amount of shearing action applied to the oil or water globules as the case may be.

Prices of machines sufficient for a pint or more:

"Empire" model	12/6
"Pentecreme" model	73/6

These prices were in force before the present war.

CHAPTER IV

GARGLES, LOTIONS AND LINIMENTS

These are all solutions intended for external treatment.

Gargles.—A Gargle (Gargarisma) is a solution intended for the irrigation of the throat, the medicament being brought

into intimate contact with the membranous lining. Because of this, oily and mucilaginous constituents should be avoided. Gargles are usually of an antiseptic or astringent character, and their preparation presents no unusual difference to that of mixtures.

As they are not for internal use, they should not be sent out in white bottles, and as they are rarely poisonous, green or blue poison bottles are hardly suitable. Such a bottle, too, might alarm the patient unnecessarily. Gargles are usually sent out in amber-coloured bottles with a coloured label. This method of packing prevents them from being mistaken for mixtures.

A solution intended for irrigation of the nose is known as a **Nasal Wash** (Collunarium), and is prepared and dispensed exactly as a Gargle.

Eye Drops and Eye Lotions.—Both these are intended for eye treatment.

Eye Drops (Guttæ oculorum) are usually aqueous or oily solutions of potent substances such as atropine, cocaine, eserine, etc., and their salts, and are intended to introduce these medicaments into the eye for mydriatic, myotic, anæsthetic and other reasons. As the eye is generally in a somewhat inflamed state and susceptible to infection, eye drops should be prepared in a sterile condition, with the same methods and precautions as for injections. When the eye is badly inflamed, the physician will often order the eye drops to be made isotonic. In this case they are to be isotonic with lacrymal secretion, which latter is isotonic with a 1·4 per cent. solution of sodium chloride (see also p. 234). The latter solution would then be used as the vehicle unless the medicament was incompatible with sodium chloride, as, for example, silver proteinate. In this case potassium nitrate could be used. Solutions of alkaloids are often prescribed in oily solution, usually castor oil, which is a good solvent for most alkaloids. Oleic acid should not be used. The powdered alkaloid is dropped into the bottle containing the castor oil (after these have been sterilized in a hot-air oven) and the stopper replaced. If necessary, it is warmed on a water-bath to aid solution.

It is essential that all aqueous solutions should be bright and clear. For the filtration, filter paper has been used for many years, but of late, the introduction of sintered glass

filters has something to commend it. These are described in the chapter on Sterilization, but a size convenient for preparation of small quantities of eye drops is known as 3 G 3 (price approx. 6*s*. 0*d*.; these filters were formerly made only in Germany, they are now made in this country).

Eye drops are sent out in distinctive bottles, and labelled "Not to be taken." There are many varieties of special eye-drop bottles suitable for providing drops. If one of these is not used, a pipette should be supplied with the drops.

Eye Lotions.—Eye Lotions (Collyria) are usually weak aqueous solutions of antiseptics or astringents, such as boric acid and zinc sulphate, and are intended for irrigating the eye. Great care should be taken to exclude foreign matter and solutions should be filtered, preferably with sintered glass. Only freshly boiled distilled water should be used as the vehicle, and the bottle and all apparatus used should be well washed with it. The use of rose water, elderflower water and similar preparations as vehicles should be discouraged, as they cannot be boiled. Eye lotions should be sent out in *stoppered* amber or fluted green bottles and labelled "Not to be taken."

Lotions.—A Lotion (Lotio) is an aqueous solution or suspension intended to be dabbed on the skin with cotton-wool or to be applied soaked in a pad of lint. They may be solutions of antiseptics or astringents, or suspensions such as Black Mercurial Lotion B.P., which contains a suspension of mercurous oxide and mercury, or Calamine Lotion B.P.C., which has calamine and zinc oxide in suspension. The preparation of Lotions usually presents little difficulty. They should be dispensed in green fluted poison bottles and be labelled "Not to be taken."

Liniments.—A Liniment (Linimentum) is a liquid or semiliquid preparation intended for external application to the skin either (*a*) by painting it on, (*b*) by friction with the hand, or (*c*) on lint. They may have an alcoholic, an oily, or a soapy base, and frequently contain camphor. They function as rubefacients and counter-irritants. Some are emulsions of an oil-in-water, such as Liniment of Turpentine. This type of liniment is often known as an embrocation. Liniments should always be dispensed in green or blue fluted poison bottles.

Inhalations (Inhalationes, or Vapores).—These are pre-

parations so designed that the patient may inhale a vapour either from a handkerchief, from a special oronasal inhaler, or mixed with the steam from hot water. They usually contain such volatile oils as pine, eucalyptus, with creosote or cresol, and such substances as camphor and menthol. Their preparation presents little difficulty, as they readily mix together. They should be sent out in poison bottles, and be labelled "Not to be taken." When the inhalation is to be mixed with boiling water and the steam inhaled, the medicaments are usually prescribed with water and light magnesium carbonate. The medicaments are added to the carbonate in a mortar, thoroughly incorporated, and then triturated with water to volume. The carbonate absorbs the oils, thus breaking it up finely when mixed with water.

Spray Solutions (Nebula).—These consist of medicaments dissolved in such solvents as liquid paraffin, glycerin, alcohol or water, and are used for spraying the nose or throat. The spray is produced by means of an "atomizer" worked with rubber bellows. When an oily base such as liquid paraffin is used, it is very important to use dry apparatus in the preparation, as a trace of water will produce a cloudy solution.

A typical spray solution is Nebula Thymol Co. B.P.C., which consists of thymol, menthol, camphor, phenol and liquid paraffin. As the solid ingredients liquefy when mixed, they should be powdered separately, placed together in a dry measure, stirred with a glass rod until liquefied, and then diluted to volume with the Liquid Paraffin. The Liquid Paraffin of the Pharmacopœia is rather too viscous for the preparation of Spray Solutions, so that the prescriber should order a less viscous variety, i.e. Paraffinum Liquidum Leve (Light Liquid Paraffin) which is now official in the Pharmacopœia, and is intended for Spray Solutions. These solutions should be dispensed in stoppered bottles and labelled "Not to be taken."

CHAPTER V

POWDERS

The physician may order substances to be dispensed in this form, and may direct that—

(*a*) A large quantity be sent, from which the patient shall measure a specified dose.
(*b*) Several doses, each separately wrapped, be sent.
(*c*) That several doses be sent, each enclosed in a special container, such as a capsule or a cachet, so as to make the medicament tasteless.

In the first two cases, the preliminary preparation of the powder is the same. The final product should be very finely powdered and in the condition known as an "impalpable" powder—i.e. one which is not gritty to the palate. Vegetable substances, such as rhubarb, senna, ginger, etc., are very difficult to reduce to this condition using a pestle and mortar. They are, however, supplied in an impalpable condition by wholesale manufacturers, who employ machinery such as edge-runner mills to produce the special degree of fineness. Crystalline substances are usually readily reduced to a fine powder using a pestle and mortar. The mortar should be of wedgwood ware and preferably not too highly polished, as the roughness of the interior surface greatly facilitates pulverization.

Compound Powders.—When several ingredients are prescribed, the following points must be observed by the dispenser:

(*a*) Each solid ingredient must be first obtained in an impalpable condition.
(*b*) The ingredients must be thoroughly mixed so that each is evenly distributed throughout the bulk powder.

The latter operation is extremely important, particularly when one or more of the ingredients is of a potent character, such as Morphia or Strychnine. Very serious consequences may follow if such ingredients are not evenly distributed. Whilst the powdering is done in a wedgwood mortar, the mixing is best done in a glass mortar using a glass pestle and

very light trituration. The ingredient prescribed in the smallest quantity should be placed in the mortar, a small quantity of one of the other ingredients added, the whole thoroughly mixed, then a little more of the second ingredient added and mixed. This gradual dilution should be carried on until all the ingredients are incorporated. Never add a small quantity of one ingredient to a large quantity of another, but always gradually dilute it and thus ensure even distribution.

When the prescriber orders a bulk quantity of some powder, such as Gregory's Powder, Compound Liquorice Powder, etc., with directions for a teaspoonful or other dose, the powder should be sent out in a wide-mouthed bottle fitted with a boxwood-topped cork or glass stopper, and bearing the directions for dosage.

The prescriber may, however, direct that several separate doses shall be sent, as in the following prescriptions :

℞. *Sodii Bicarb.* gr. v.
Pulv. Zingiber. gr. iii.
Misce. Fiat pulvis. Mitte xii.

This means that 12 powders must be sent, each containing 5 gr. of sodium bicarbonate and 3 gr. of powdered ginger. The procedure is as follows : Calculate for 13 powders so as to allow for loss due to powder adhering to the mortar, scale pan, etc. Thus $5 \times 13 = 65$ gr. of sodium bicarbonate and $3 \times 13 = 39$ gr. of powdered ginger would be weighed out, thoroughly mixed in a glass mortar, using the light "mixing" action of the pestle (Fig. 14). From this, 12 powders each weighing $5 + 3 = 8$ gr. would be weighed and separately wrapped in paper.

The bulk of a powder varies. Generally prescribers order not more than 20 to 40 gr.—often about 5 gr. are prescribed. The final bulk should not be less than 2 gr. as it would then be too small to be handled by the patient. Should the actual quantity of medicament be less than 2 gr. it is usual to dilute it with some inert substance such as lactose in order to make it more bulky.

The student should carefully note the following prescription :

℞. *Calomel* gr. $\frac{1}{6}$.
Fiat pulvis. Mitte x.

This requires each powder to contain $\frac{1}{6}$ gr. of calomel. The actual quantity is too small for a single powder and must be made up to, at least, 2 gr. The procedure is as follows :

Weigh $12 \times \frac{1}{6} = 2$ gr. of calomel, and 22 gr. of lactose. These represent the quantities for 12 powders, 12 being selected because of the convenience in weighing the calomel. Thoroughly mix, taking all the precautions regarding dilution, and weigh out ten 2-gr. powders.

℞. *Acid. Arseniosi* gr. $\frac{1}{50}$.
Fiat pulvis. Mitte xii.

This prescription presents another problem. Each powder must contain $\frac{1}{50}$ gr. of arsenic, and, calculating for 13 powders, the total quantity would be $\frac{13}{50}$ of a grain. Now $\frac{13}{50}$ gr. is too small a quantity to weigh, therefore a dilution or triturate must be made. Weigh 1 gr. of arsenic, make it up, with very careful dilution, to 50 gr. with lactose (i.e., add 49 gr.) and weigh out 13 gr. of the mixture. This 13 gr. will contain $\frac{13}{50}$ gr. of arsenic, but as the total weight of 13 powders must not be less than 26 gr. (i.e., 2 gr. each), a further 13 gr. of lactose must be incorporated and twelve 2-gr. powders weighed out.

℞. *Ol. Menth. Pip.* ♏i.
Pulv. Rhei gr. iii.
Sod. Bicarb. gr. v.
Misce. Fiat pulvis. Mitte xii.

This is an example of a powder containing a volatile ingredient. Calculate for 13 powders. The powdered rhubarb should be placed in the mortar, the oil of peppermint dropped on, and well incorporated by trituration. Finally, the sodium bicarbonate should be added and mixed. Reckoning 1 minim of the oil to be equal to 1 gr., twelve 9-gr. powders should be weighed out. The powders should be first wrapped in greaseproof or wax papers, to prevent loss of oil by volatilisation, and finally in white paper.

The white paper used for powders should be glazed (known as white glazed demy), and for small powders about 4×5 inches is a convenient size, and preferably machine-cut rather than hand-cut, it being so much neater. To fold a powder requires a good deal of care and practice, and once

learned it is never forgotten and is useful when applied to many other little operations. Though so simple, it is, however, a difficult task to describe in writing. Fig. 16 shows the preliminary steps for the folding of powders weighing up to about 60 gr. each. The dispenser places the paper before him on the counter or table with the powder in its centre, and brings the border of the paper farthest from him to within half an inch of the border next him; he secures it in this position with his index-fingers, whilst with his thumbs he turns the half-inch of margin of the paper next him in a flap over it. This is again folded over on itself, which completes the folding (Fig. 16), the ends being turned down, as in the first instance, by the fingers, over a knife or on a powder-folder.

A represents the farthest edge brought towards the folder; in B the edge next him is turned over in a flap upon this; in C and in D both are together turned over in a second flap; and the folding is completed by turning the ends back. The dotted lines show the space originally covered by the paper. In this method the powder is technically said to be folded "to" the dispenser. More commonly, however, it is folded "off" him, and this is the proper way, only it is more difficult to accomplish for the first time. It is done precisely in the same way, except that the near edge of the paper is brought to within half an inch of the farthest edge, which is turned over on it, and again both are turned over as before.

The following still simpler method of folding a powder may be easily mastered by the student:—He places the paper before him with the powder in its centre, and turning back into a flap about half an inch of the margin next him, he smooths it down flat upon itself. Into the crease of this flap he inserts the edge of the paper farthest from him, and bends both over exactly as in the two previous instances, and finishes the ends as before.

The length of the powders can be kept constant by using a powder-folder which can be adjusted to the correct distance to suit the box into which they are to be put (Fig. 16, D). The width must be judged by eye. The wrapped powders should be placed together neatly, bound with an elastic band, and placed on their *edges* in the box. They should not be so wide as to protrude above the level of the box.

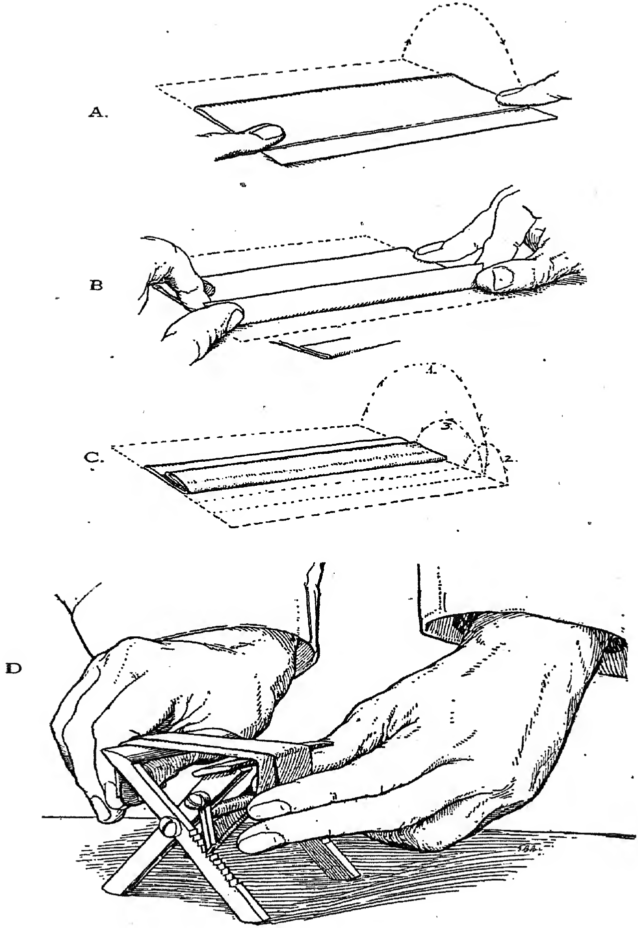


FIG. 16.

Small quantities of powders are sometimes dispensed in a small envelope instead of a box.

Powders for External Use.—Bulk powders are sometimes ordered for use in the preparation of **Lotions**—for example, 1 oz. zinc sulphate, with directions that so much of it shall be dissolved in a quantity of water and used as directed. Such powders should be either (*a*) wrapped in blue or red paper with a red label, and, in addition to the directions, should bear the words "Not to be taken"; or (*b*) in a green or blue wide-mouthed, wood-topped poison bottle and similarly labelled.

Solvellæ.—Powders intended for lotions are now replaced in part by Solvellæ or solution tablets. A certain number of these are official in the B.P.C. and are compressed tablets intended to be dissolved in water for external or local use. In the preparation of these tablets all ingredients, including lubricant and diluent, must be readily soluble in water. Thus sodium chloride is often used as a diluent and boric acid as a lubricant. When they contain poisonous ingredients, a dye is also added so that the tablets are distinguishable.

The B.P.C. directs that where the proportion of medicament to be contained is not stated by the prescriber, the following quantity shall be dispensed

Solvellæ Acidi Borici :—Boric acid, 1 gm. (15 gr.)
,, Aluminis :—Alum, 0·6 gm. (10 gr.)
,, Potassii Permanganatis :—Potassium Permanganate, 0·3 gm. (5 gr.)
,, Sodii Chloridi :—Sodium chloride, 1·3 gm. (20 gr.).

Amongst the official solution tablets, the following are important.

Solvellæ Antisepticæ.—Effervescing mouth-wash tablets, a tablet of sodium bicarbonate, borax, sodium benzoate and boric acid, with menthol, thymol and oils of eucalyptus and lemon. The tablet is coloured pink with eosin and carmine.

Solvellæ Hydrargyri Iodidi.—Soluble biniodide tablets. These contain mercuric iodide and potassium iodide coloured pink with eosin. Mercuric iodide, although insoluble in water is readily soluble in solutions of potassium iodide. One tablet dissolved in a pint of water yields a solution 1 in 1,000 of mercuric iodide.

Solvellæ Hydrargyri Oxycyanidi.—Mercuric oxycyanide

solution tablets. These are also coloured pink with eosin and are of such a strength that one tablet dissolved in a pint of water will yield a solution of mercuric oxycyanide 1 in 2,000.

Solvellæ Hydrargyri Perchloridi.—Mercuric chloride solution tablets. These are coloured blue with methylene blue, and when one tablet is dissolved in a pint of water it yields a 1 in 1,000 solution of mercuric chloride.

Dusting Powders (Pulvis conspersus).—These must be made extremely fine so that they can be used in a "dredger" or cylindrical box with a muslin end. They often need very careful preparation, as the ingredients are sometimes difficult to distribute. The following are common ingredients—camphor and spermaceti: These are best powdered by adding a few drops of alcohol, which causes the pestle to grip. Zinc oxide and salicylic acid: These need very careful powdering. Volatile oils and tinctures: These liquids must be first well absorbed by one of the solid ingredients and then carefully diluted with the remainder. Carmine is often added to colour the powder, and it requires some experience to get it evenly distributed. A very small quantity only is usually ordered, and it should be dropped on to some other ingredient, starch for preference, and very *lightly but thoroughly* incorporated. Only then may it be diluted with the other ingredients. The student should remember that *every* solid ingredient should first be separately powdered as fine as possible, the whole then mixed together (small quantities being gradually diluted), and the final powder should be passed through a suitable fine sieve. It should be packed in a "dredger."

Tooth Powders.—The preparation of these resembles dusting powders. They should be packed in wide-mouthed, wood-topped bottles or special tins.

Snuffs (Insufflationes).—These are very light powders intended for snuffing up the nose in the usual manner or by means of a special piece of apparatus known as an insufflator. They may have a basis of starch, lycopodium, or boric acid, and be medicated with a variety of substances such as menthol, cocaine, morphine, etc. Their preparation resembles that of dusting powders, and they are generally dispensed in flat pill-boxes.

CHAPTER VI

CACHETS, CAPSULES, TABLETS, EFFERVESCING GRANULES

Cachets provide a very excellent method of administering powders, and are particularly useful for nauseous or bitter substances, such as quinine sulphate, etc. They are made from a flour-and-water paste, dried to wafer thickness and moulded to cell shape. When wetted in water, they readily soften to a pulpy mass, which is easily swallowed.

There are many sizes of cachets, each being distinguished by a number, and the dispenser should always choose the smallest possible one which will hold the powder.

There are two main types on the market, the *dry closing* and the *wet closing*.

Dry-closing cachets are extremely easy to fill, and dispensers are recommended to adopt this type. The medicament is placed in one half of the cachet and the top part placed on. The latter slides on to the lower half, just like the lid of a pill-box. Very little skill in manipulation is required, and in comparison with the wet-closing type, much time is saved.

The use of a wet-closing cachet machine requires more practice. The cachets for this type have rims which are wetted prior to being stuck together. The machine (Fig. 17) is composed of three plates on hinges (A, B, and C), which with the funnel (D), thimble (E), and felt roller (F) for moistening the rims of the cachets, complete the apparatus.

The powders should be first prepared and weighed out on to papers, exactly as though they were going to be wrapped. Crystalline substances, however, need not be powdered. Suitable-sized cachets are chosen, half being put into holes in plate C and the others into the corresponding depressions in plate A; the middle plate (plate B) is now hinged over to cover plate A. The funnel on being placed in position rests on the edge of the hole in plate B so as to avoid pressing upon the cachet and also to allow sufficient elevation of the powder when pressed in to fill the upper cachet when it is ultimately brought to cover it. A powder is placed in the funnel, and with the thimble (E) upon the index-finger the

drug is pressed lightly downward into the cachet. The end of the thimble is concave, so that the surface of the contents is convex. This process is repeated until all the powders have been inserted. Plate B is now hinged off and the filled half cachets or "cachet-leaves" are ready to receive the others to complete the process. This next step is the one which requires most skill, for the application of moisture to the rims is important. Neither too much nor too little should be applied. If too much, the rims are likely to shrivel;

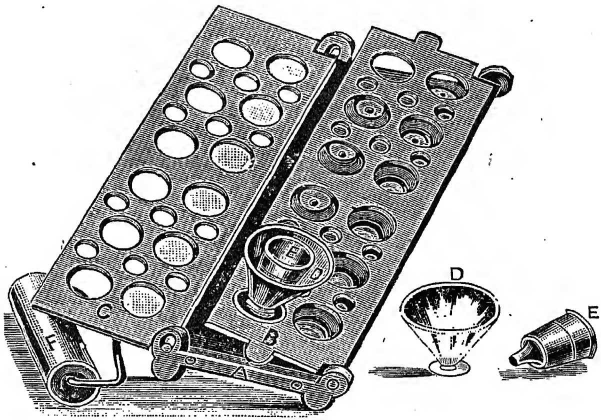


FIG. 17.

if too little, they will not stick together. To moisten the rims the roller (F) is damped by passing it over a wet felt pad, and then it is rolled over the rims of the half cachets in plate C, which is then hinged over and pressed upon plate A. The finished cachets are gently removed from the circles in plate C, and are dispensed in boxes. They should never be packed in cotton-wool, as this might stick to the damp rim. In addition to the directions for dosage, the box containing the cachets should bear directions stating how they should be used. Suitable directions are: "Immerse the cachet in water for a few seconds and then swallow with the water."

The dry-closing machine is very similar in design and in manipulation except that no damping is required, the cachets sealing by gripping together, thus avoiding a big difficulty for a beginner as well as quickening the process.

Capsules.—Whilst cachets are only used for enclosing solid medicaments, capsules may be used for solids, semi-solids or liquids. They are made with a gelatin base with a varying amount of glycerin according to the degree of hardness required, for they are made (*a*) soft and flexible, usually oval in shape, for liquids and soft masses, and (*b*) hard for powders.

Hard Capsules are made in two halves, one fitting lightly over the other like a lid, the whole being cylindrical in shape. The powder is fed into the lower half, generally through a small funnel, and tamped down with a glass rod. The cap is then moistened on the inside with water by means of a camel-hair brush and placed on the other half, to which it adheres, the capsule thus being sealed. When soft substances, such as a soft extract or ichthammol, are ordered to be placed in a hard capsule, they should be treated as in the making of pills—made into a mass with an excipient, rolled, cut, but not rounded. The cut pieces should be inserted in the capsule and the cap sealed on. Soft *aqueous* extracts or masses tend to soften the gelatin, so that it is advisable to incorporate a trace of soft paraffin in the mass prior to filling the capsules.

Soft Capsules are usually oval in shape and are supplied with a fairly long neck and sealed. The filling of a soft capsule requires some degree of practice, particularly if an oil is the liquid to be handled. For small quantities on the dispensing counter, probably a hypodermic syringe is the best thing to use. The neck of the capsule is cut and a measured quantity of the liquid put in. Care should be taken (particularly if oil has been used) not to wet the lip of the capsule, as this will make sealing difficult. The sealing may be done in two ways: (*a*) By leaving a long neck on the capsule and melting this with a hot glass rod or steel spatula. With experience, quite a good seal can be obtained. (*b*) Leaving a short neck and placing on it a blob of melted glycogelatin from the end of a glass rod. The melted glycogelatin can be obtained by placing a few soft capsules in an evaporating dish with a few drops of glycerin, and melting on a water-bath. The student

should practice sealing empty capsules until he is satisfied with the appearance of the finished article.

Aqueous liquids must be concentrated if possible to low bulk and emulsified in some oil, such as almond oil or liquid paraffin, before capsuling. Some liquids, like Oil of Cloves and cinnamon, creosote, etc., may cause great discomfort in the stomach if dispensed in a capsule alone, and to avoid this, they should always be mixed with four times their volume of oil (such as olive or almond). Substances such as Extract of Male Fern, pancreatin, etc., which must pass through the stomach into the intestines unchanged, can be capsuled, and the capsules converted into " glutoid capsules " by immersing in a solution of formaldehyde in exactly the same manner as the preparation of a " glutoid " coating on gelatin-coated pills (see p. 201). The finished " glutoid capsules " should conform to the same disintegration tests as the pills.

Hard and soft capsules are supplied by manufacturers in many varied sizes. The dispenser must always choose the *smallest* size for his purpose. The name " Perles " is given to spherical capsules which have been filled and sealed in a special machine, but their preparation is not practicable on the dispensing counter.

Tablets.—Tablets represent a very popular modern method of exhibiting medicaments by compressing a powdered drug in a machine and forming a more or less hard mass. The degree of compression varies according to the type of tablet required. In some cases (e.g. acetylsalicylic acid) just sufficient compression is used to form a tablet which will retain its shape whilst being handled and packed, but which can be readily crushed before being swallowed with a draught of water. On the other hand, some medicaments (e.g. potassium chlorate) require to be slowly dissolved in the mouth, and much greater compression is used and a very hard tablet is produced. Such tablets are really lozenges.

The dispenser is rarely called upon to prepare tablets at the dispensing counter, and a full account of the process is out of place here. A powder cannot, as a rule, be directly compressed into a tablet, but must be made into small granules which, when compressed, interlock and form good tablets. Small, hard crystals will do the same. In the preparation of the granules the powdered medicament is made into a mass which will readily clog by damping with some liquid such as

simple syrup or Mucilage of Acacia (or a mixture of these), passing through a sieve, drying the resulting granules in a hot-air oven, and again passing through the sieve, any fine powder being sifted out. In order to prevent the granules from adhering to the punches in the machine, a small quantity of talc is often added to the finished granules.

Tablet Triturates.—These are very small tablets, usually containing very potent ingredients and capable of being either easily powdered or readily dissolved in water. They generally contain a basis of lactose, and are prepared by very light compression. Hypodermic tablets for the preparation of injections are made by this method.

Effervescing Granules.—These consist of granules prepared from a mixture of the medicament with citric and tartaric acid, sodium bicarbonate and usually some sugar. Such a mixture when gently warmed on a water-bath softens and clogs together owing to a slight interaction between the acids and bicarbonate, with the production of a little water and some carbon dioxide. The latter aerates the mass, so that on further drying and careful manipulation light porous granules are obtained, which, when added to water, effervesce briskly and provide a pleasant medicated draught. The Pharmacopœia contains two effervescing granular preparations, Effervescent Sodium Phosphate and Effervescent Sodium Sulphate.

CHAPTER VII

OINTMENTS

OINTMENTS are preparations made with a fatty base and intended for external application. They may be required to exert merely a soothing emollient action, in which case no medicament is required. Usually, however, the fatty basis serves as a vehicle for some medicament which may be required to exert a local surface action on the skin (e.g.

boric acid, salicylic acid, and Phenol ointments), or to be absorbed through the skin (e.g. mercury and belladonna ointments).

The usual ointment bases consist of lard, wool fat, soft paraffin, or a mixture of hard and soft paraffin.

Lard (Adeps) is the purified abdominal fat of the pig, and is one of the oldest of ointment bases. Being an animal fat, it is readily absorbed by the skin, and is therefore generally thought to be suitable for such medicaments as are required to be absorbed. Its chief disadvantage is its tendency to go rancid, and to counteract this benzoinated lard (Adeps Benzoinatus) is often used. This is prepared by digesting melted lard with powdered benzoin for one hour at 60° C., then straining and stirring until cold. The aromatic acids in the benzoin are dissolved out, and tend to prevent rancidity developing in the lard on keeping.

Wool Fat, or **Anhydrous Lanolin** (Adeps Lanæ), is the purified fat obtained from sheep's wool. It is a firm, yellowish-brown fat, rather too sticky to be used by itself as a base, and is therefore usually mixed with some other base, such as the paraffin type. Like lard, wool fat is readily absorbed by the skin, but its most characteristic property is its power to emulsify water and aqueous solutions or extractives. If much aqueous liquid has to be incorporated in an ointment, wool fat is usually included in the formula.

Hydrous Wool Fat, or **Lanolin** (Adeps Lanæ Hydrosus), consists of water (30 per cent.) emulsified in wool fat (70 per cent.). It is softer and less sticky than wool fat alone, and is a good emollient base.

Paraffin.—The paraffin type of base consists of either soft paraffin (Paraffinum Molle) or a mixture of this with hard paraffin (Paraffinum Durum or Paraffin Wax). Paraffin ointment is a mixture of soft and hard paraffins and a little white beeswax. A paraffin base never goes rancid, and is but slowly absorbed through the skin. For the latter reason it makes an excellent base for such medicaments as salicylic and boric acids, which are required to exert only a surface action. Another advantage of this base is the fact that the consistency can be varied by altering the proportions of hard and soft paraffin. As two varieties of soft paraffin are official, the Pharmacopœia lays down the ruling that when the medicament

is white or colourless, then the white variety of soft paraffin shall be used, and when the medicaments are coloured, the yellow variety.

Simple Ointment (Unguentum Simplex) consists of a mixture of wool fat (5) with hard paraffin (10) and soft paraffin (85). It was introduced into the present Pharmacopœia to replace lard in many ointments. Unlike the latter, it does not go rancid, whilst the presence of some wool fat ensures a certain amount of absorption through the skin and imparts to it the property of taking up or emulsifying quite an appreciable amount of aqueous fluids. It serves as a very useful general base.

The Preparation of Ointments.—In the preparation of ointments the student should always bear in mind that the medicaments should not only be evenly distributed throughout the base,. but must be, if possible, dissolved in the base. If the latter condition is not possible, then they must either be dissolved in water and the solution emulsified in the base or levigated down to a very smooth powder and suspended in the base. The student should first consider the possibility of bringing the medicament into actual solution, but great care must be exercised, for, whilst it may be soluble in the melted base, it may crystallize out on cooling. Such crystals may be the cause of much irritation when the ointment is applied to the skin. Should crystallization be possible, the student would be well advised to treat the medicament as an insoluble one, finely powdering it and incorporating it in the cold basis.

The procedure, when the medicament is soluble in the base, is a very simple one, both being placed in a porcelain dish or an ointment pan, gently heated on either a water-bath or sand-bath, and stirred constantly until solution is effected. The vessel is then removed from the bath and the ointment stirred until cold.

When the medicament is insoluble, the operation may be carried out on either a porcelain ointment slab or in a large mortar. The following procedure should be followed: All solid ingredients should be finely powdered *separately*, then well mixed together and finally passed through a fine sieve. The powder or mixed powders should then be well levigated down with a little of the fatty base. If a slab be used, levi-

gation is carried out with a large flexible steel spatula (if interaction between the medicament and steel is possible, a stainless steel spatula should be used). Should a mortar be used, levigate with a very flat-headed pestle. Generally speaking, finer levigation is obtained on a slab than in a mortar. When levigation is completed, the rest of the base should be gradually incorporated and the whole thoroughly mixed. Any extracts in the formula should be rubbed down to a thin paste with water, alcohol, or glycerin and then incorporated. Medicaments which are freely soluble in water should be dissolved in a small quantity and the solution dispersed in the base.

The preparation of ointments is not a simple operation, although it may appear very easy, and it cannot be too strongly emphasized that all ointments should be most carefully prepared, great precautions being taken to produce a smooth preparation entirely free from gritty particles. It is not uncommon to see sores irritated and eyes inflamed by the very remedies prescribed to soothe them.

Ointments may be packed in pots with celluloid lids, in wide-mouthed amber glass bottles with screw lids, or in collapsible tubes.

Eye Ointments (Oculenta).—These are so important that it is well to consider them as a special class of ointment. The Pharmacopœia gives general directions for their preparation and prescribes a mixture of yellow soft paraffin and 10 per cent. wool fat as the basis. The base is melted and filtered whilst hot through coarse filter-paper placed in a heated funnel (or the whole placed in a hot-air oven) and then sterilized by heating in a hot-air oven at 150° C. for one hour. If the medicament is an alkaloidal salt, it is dissolved in a little distilled water and incorporated in the sterile basis. If the medicament is not water soluble it should be finely powdered in a sterilized mortar, levigated with a small quantity of the sterile base and then mixed with the remainder. Eye ointments should always be prepared under aseptic conditions and should not be packed in pots or bottles, but in sterile collapsible tubes. This method of packing reduces the risk of reinfection of the ointment.

Pastes.—Although these do not contain fats and are of a non-greasy character, they are included here because their use

is similar to that of ointments—i.e. they provide a method of keeping medicaments in prolonged contact with the skin. The bases may consist of—

(*a*) Glycero-gelatin as in gelatin of Zinc B.P. or Unna's paste. For use, such a paste has to be melted by standing the container in hot water, spreading the melted mass on lint and applying to the skin whilst still soft.

(*b*) Glycerin of Starch B.P. Zinc oxide, starch and salicylic acid are often ordered to be incorporated with it.

(*c*) Soap. The Liniment of Potassium Iodide with Soap of the 1914 Pharmacopœia has a soap basis and is used like an ointment.

(*d*) Bassorin Paste. This is a mixture of glycerin and tragacanth and is used like glycerin of starch.

The preparation of these pastes is similar to that of ointments; all insoluble solids must be thoroughly powdered and well levigated with a little of the base before dilution. Zinc oxide is a frequent source of trouble because of grittiness, but a good quality product gives less trouble in this respect than a cheap sample.

CHAPTER VIII

PILLS

PILLS provide a very useful method of exhibiting certain medicaments, being compact and convenient and capable of being so coated as to be tasteless. The ingredients, as a rule, retain their activity for a long time. Pills vary very much in size, weighing from 1 to 5 gr., but occasionally heavier when the medicaments are of a dense nature and do not make an abnormally large pill. When the ingredients have been massed together and rolled into pill form, the following requirements must be met:

(*a*) The pills must disintegrate in the stomach (or intestines).
(*b*) The constituents must not be altered during the process of making the pill, and must be evenly distributed throughout the mass.
(*c*) The pills must retain their shape.
(*d*) The pills should be of even weight and elegant in appearance.

Excipients.—Should none of the medicaments be suitable for producing a mass, some substance, known as the excipient, must be added. The choice of the excipient is often left to the dispenser, and this requires a certain amount of experience, as, whilst it may produce a good mass, it must not alter the activity of the ingredients nor make the mass insoluble when taken.

The following liquid excipients are in common use : water, simple syrup, Syrup of Liquid Glucose, liquid glucose, alcohol, wool fat. In certain cases it may be necessary to use other auxiliary excipients along with these liquid excipients, such as powdered gums, to give greater adhesiveness to mass, or absorbents such as liquorice root, kaolin, calcium phosphate, kieselguhr or powdered soap.

Water will form a good mass if the ingredients contain substances of a gummy nature. It will form a good mass with Aloes.

Simple Syrup is not very binding, but it forms a very soluble mass.

Liquid Glucose is very binding, forming a good mass which, because the excipient is slightly hydroscopic, never goes very hard on keeping. Owing, however, to its great viscosity, it is a very difficult excipient to work into the mass.

Syrup of Liquid Glucose is one of the best excipients. It is much easier to work than liquid glucose ; forms a readily soluble mass, which does not unduly harden on keeping.

Alcohol is a useful excipient for pills containing much resin, such as podophyllin or scammony. Some of the resin dissolves in the alcohol, forming a pasty mass which binds the remainder of the resin together, the alcohol finally evaporating. In order to retard the rate of evaporation of the alcohol it is often an advantage to add a trace of glycerin to it.

Wool Fat is useful for—

(*a*) Massing resins such as podophyllin or scammony.

(*b*) Massing substances, such as potassium permanganate, potassium dichromate or silver nitrate, which, being rich in oxygen, cannot be massed with the usual excipients because they interact.

Wool fat usually requires the addition of a little calcium phosphate, kaolin or kieselguhr.

Powdered Liquorice Root is useful in providing fibre and thus facilitating massing with a liquid excipient such as Syrup of Liquid Glucose. It may be used to stiffen soft masses.

Powdered Hard or Animal Soap.—Useful for absorbing volatile oils such as peppermint, creosote, etc. It is usually necessary to stiffen with liquorice, kaolin, calcium phosphate or kieselguhr.

Compound Acacia Powder.—A mixture of equal parts of powdered gum acacia and tragacanth. It is a very useful addition to introduce binding qualities into a mass. As a rule not more than 5 per cent. should be used, otherwise the mass becomes rubbery when the liquid excipient is incorporated and will be difficult to shape and round.

The following is a general scheme for the choice of excipient, and the student will find that there are very few substances to which the scheme cannot be applied. The student should always bear in mind that success in producing suitable pill masses only comes by long practice, and very often failure to produce a good mass is due to manipulation and not to the excipient.

Rules for Excipients :

1. When the ingredients contain binding material such as fibres from vegetable powders (e.g. powdered rhubarb) or gummy material (e.g. aloes), use Syrup of Liquid Glucose.
2. When the ingredients contain no binding material as above, such as chemical compounds (e.g. potassium bromide, camphor, sulphur, etc.), incorporate 5 per cent. Compound Acacia Powder and mass with either Syrup of Liquid Glucose or liquid glucose.
3. When the ingredients are of a resinous nature, such as

podophyllin, jalap, scammony, mass with 90 per cent. alcohol containing a trace of glycerin.

4. When the ingredients are very rich in available oxygen, such as potassium permanganate, etc., make into a very stiff paste with wool fat and stiffen with kaolin.
5. When ingredients are of an oily nature, such as oil of peppermint, croton oil, or creosote, thoroughly incorporate in powdered animal soap (1 gr. of soap for 1 min. of oil) and stiffen with liquorice powder.

Preparation of the Mass.—The dispenser having read over the prescription and selected the excipient which he will use (if such is not already directed by the physician) proceeds to weigh out the different ingredients, taking the substances that require pulverization first. When small quantities of a potent substance such as arsenic or strychnine are required, the preparation of a triturate will be necessary, and the dispenser, having finally weighed out the requisite amount of this, must dilute it with the other ingredients of the prescription, taking exactly the same precautions to ensure even distribution as in the preparation of powders (see p. 178). When all the dry substances have been added and thoroughly mixed, any soft extracts should be incorporated and the mass worked up with the excipient in a mortar, incorporating only small quantities at a time. The proper mortar should be of good wedgwood ware, shallow, and small enough to be firmly grasped in the left hand. A small, long-handled pestle should be used in the manner described on p. 162 (Fig. 15). By vigorous manipulation the heat produced by the friction so softens the mass that less excipient is necessary to produce a workable pill. A properly prepared mass will usually come out of the mortar readily and not stick to the bottom or to the pestle.

Rolling.—When the mass is of the right consistency, it is scraped out of the mortar with a small stiff spatula, and it is a good plan to work it for a few minutes between the fingers in order to soften it. It is next rolled into a ball or cylinder with the finger and thumb and transferred to the slab of the pill machine, which should previously have been smeared with a trace of French chalk. The back of the handle of the machine is used to roll it into a long cylindrical form (the pipe), great care being taken to produce a cylinder of even

dimensions and not tapering out thin at either end. The ends should be square and not rounded. The handle of the machine should be held perfectly horizontal, as shown in the sketch (Fig. 18), and each hand bearing an equal weight on the mass as it is rolled backwards and forwards over the slab. The pipe is brought from time to time alongside the scale, and, when the number of pills into which it is to be divided corresponds to the number marked there, it is gently lifted or rolled with the fingers on to the grooved part of the machine; the handle, with its grooved surface downwards, is laid on it,

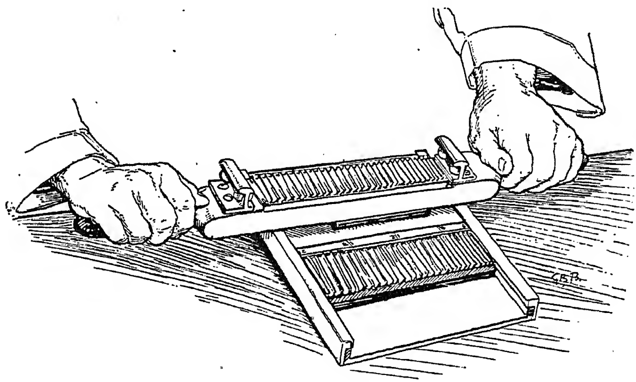


Fig. 18.

and by a series of rapid and short movements (with both hands) abruptly brought to a close by pushing the handle from the dispenser, at the same time turning it on its own axis in his hands, the cylinder is cut and rounded into globular pills, which, with the last motion, are pushed into the box or tray at the end of the machine. If the operation is successful, and the mass of good consistence, no further handling will be necessary; but generally the track of the machine will be visible on each pill, and another process is required before the smooth globular form is perfect.

Rounding.—The pills are again placed on the dusted slab and covered with a pill-finisher—which is a circular shallow

boxwood tray, not so deep as the pills—and by a series of rapid rotatory movements the traces of the machine are dispelled and a more spherical and polished appearance is given (Fig. 19). A trace of French chalk may be necessary during the operation, but it should always be rubbed on the machine and finisher, never sprinkled on the pills. Excess must be avoided, as otherwise, instead of obtaining a fine polished surface, the pills will have a dull, dusty appearance.

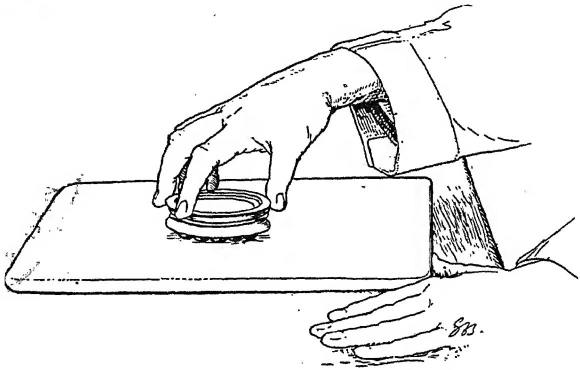


FIG. 19.

Coating.—The prescriber may direct that the pills should have a special coating, or in the absence of such directions the dispenser may decide that one is necessary. Pills are coated for one or more of the following reasons :—

1. To make them tasteless, and thus disguise nauseous or bitter medicaments.
2. To protect the mass against changes, such as—
   (*a*) The loss of volatile constituents, as a volatile oil, camphor, etc.
   (*b*) Oxidation, as in the case of pills containing ferrous carbonate, phosphorus, etc.
3. To improve the appearance of the pills.
4. To give them a special enteric coating which will permit the pill to pass unchanged through the stomach and

yet dissolve in the alkaline medium of the intestine. Enteric coating is becoming increasingly important, and is particularly valuable for the following classes of medicaments :

(*a*) Those which would be inactivated if liberated in the stomach, such as pancreatin.

(*b*) Those which, in order to be effective, are required to reach the intestines in a concentrated form, such as anthelmintics like santonin, thymol, Extract of Male Fern, pelletierine tannate.

For purposes 1, 2, or 3, the pills may be varnished, sugar coated, pearl coated, or gelatin coated. Silver coating is used merely to give an elegant appearance to the pill, and serves no useful purpose. Its use is rapidly diminishing.

Varnish Coating.—The varnish usually employed consists of a 1 in 4 solution of sandarac in either absolute alcohol, or a mixture of alcohol and ether. The latter would give a quick-drying varnish and the former a slow-drying varnish. The operation of varnishing is carried out as follows : An ointment tile is prepared by smearing a trace of some oil such as olive or almond. The pills, which should be quite free from powder and preferably highly polished, are placed in an ointment pot, and a few drops of the varnish solution added. The pills are then rapidly rotated in the pot for a few seconds and quickly thrown out on the oiled slab, any sticking together being immediately separated with a long needle. After a few minutes each pill is turned over with the needle, so that there shall be no contact mark upon them. The trace of oil on the slab prevents the varnish from sticking to the slab. The pills should be allowed to remain on the slab for about half an hour to dry thoroughly.

A sandarac varnish coating forms an excellent coating for nauseous or bitter medicaments or to protect volatile or oxidizable ingredients.

Silver Coating consists of covering the pills with very thin silver leaf. The pills are placed in the palm of the left hand, which has previously been smeared with a little weak mucilage of acacia. They are then rotated with the fingers of the right hand until evenly coated with mucilage and until the mucilage has become nearly dry or tacky. They are then quickly thrown into a pot containing the silver leaf (one leaf for every

5 or 6 pills) and rapidly rotated for several minutes. They should then be transferred to another clean, dry pot, excess of leaf being left behind, and again rotated. Finally, they should be placed upon a pill-finisher and well burnished by being gently rotated with the hand covered with a piece of soft tissue paper.

Silver coating requires some experience, and success usually only comes after much practice. The secret lies in getting to know the right degree of "tackiness" of the mucilage coat before rolling in the silver leaf. If the pills are too wet, the silver coat will be very dull and too much leaf will be required. If, on the other hand, the pills are too dry, they will be irregularly coated. Should the pills contain substances which react with silver, such as sulphides, mercury, etc., they should be varnished before being silvered.

Sugar Coating consists of building up a thin layer of sugar on the pill, and if properly done provides a very excellent protective coat which is readily soluble. It can rarely, however, be carried out on a dispensing counter, for to be successful it requires a large number of pills to operate upon. The pills are gently rotated in a special globular pan in a current of warm dry air, syrup and powdered sugar being added from time to time. After the coating of sugar has been built up, they are finally burnished in a rotating wax-lined pan.

Pearl Coating consists of building up a layer of talc or French chalk with mucilage of tragacanth or acacia (the former is preferable, producing a whiter coat). Pearl coating can be carried out on a small scale, but it is not to be recommended, as it often produces an insoluble layer, preventing the subsequent disintegration of the pill. It is often carried out on a commercial scale as an imitation sugar coating, being sweetened with Saccharin. The practice should be condemned.

Gelatin Coating.—This is one of the best types of coating, and is done by dipping the pills in a solution of gelatin in water containing a little glycerin to make the film flexible. On a small scale it is done by impaling the pills on the end of a series of needles set upright in a piece of wood or cork. This arrangement is then inverted and the pills lowered into the gelatin bath, then reversed. Excess of gelatin flows down the needles and the pills are allowed to dry. A special machine is used on a large scale.

Enteric Coatings are special coatings intended to render the pill insoluble in the acid juices of the stomach, but allow it to disintegrate in the alkaline media of the intestines. Before being passed as satisfactory they should be tested by being immersed in a solution of pepsin in water acidulated with hydrochloric acid, and kept at body temperature (37° to 38° C.) for 2 hours, with occasional shaking. They should not disintegrate. They should next be placed in a solution of pancreatin in water made alkaline with a little sodium bicarbonate and again maintained at body temperature for 2 hours with occasional shaking. The pills should disintegrate within 2 hours. Many of the so-called enteric coatings are useless. Probably the most efficient is one prepared by immersing ordinary gelatin-coated pills in Solution of Formaldehyde B.P. for 10 minutes, then removing and drying. The formaldehyde reacts with the gelatin, forming a compound which has all the requirements of an enteric coating. Such a coating is often known as a "*glutoid*" coating, and the method has the advantage of being easily carried out. The time of immersion in the formaldehyde solution is very important, as too long immersion will render the coating insoluble in either acid pepsin or alkaline pancreatin solution, whilst with insufficient immersion the coating will not resist an acid pepsin solution.

Other methods for producing enteric coatings include coating the pills with salol, stearic acid, or keratin, but all these are more difficult to perform, and the result is rarely as satisfactory as a "glutoid" coating.

CHAPTER IX

SUPPOSITORIES, PESSARIES AND BOUGIES

SUPPOSITORIES, Pessaries and Bougies are very similar in their preparation and function. They are intended for the introduction of medicaments into the rectum (suppositories), the vagina (pessaries), the urethra (urethral bougies), the nose (nasal bougies), or the ear (aural bougies). They

are all made with a basis of either Oil of Theobroma (cacao butter) or glycero-gelatin, which consists of a mixture of gelatin, glycerin and water. The basis must have the following characters: (*a*) It must melt below body temperature, 37·8° C.; (*b*) it must be sufficiently hard at ordinary atmospheric temperature to be readily handled. Unless otherwise specified, Oil of Theobroma should be used for the basis, as it is particularly suitable for the purpose, its melting-point being 31° to 34° C., whilst at ordinary temperatures it is a hard wax. It is very important to remember, however, that should Oil of Theobroma be overheated, its melting-point is lowered and the theobroma does not readily solidify again. Consequently if heat is necessary for the incorporation of the medicament, only the minimum amount should be used to melt the Oil of Theobroma, otherwise difficulty will be experienced in getting the mass to solidify in the mould.

Suppositories (Suppositoria) are of two shapes, cone-shaped or torpedo-shaped, and usually weighing about 15 gr. (1 gm.), although 30-gr. and 60-gr. ones are occasionally required.

They are made in silver-plated brass or copper moulds by cold compression or by being poured in as a melted mass and allowed to solidify. The cold compression method can only be used for theobroma suppositories, and is usually only carried out on a manufacturing scale with a specially designed machine which is rarely seen on the dispensing counter.

The Mould.—The moulds should be carefully handled and should never be scraped with a knife or spatula, but should be cleaned by immersing them in warm water and afterwards wiping dry. If the plating becomes scratched the appearance of the suppositories will suffer.

Capacity and Displacement.—The capacity of the mould is usually stamped upon the side and refers to Oil of Theobroma only, for whilst a 15-gr. mould will hold 15 gr. of theobroma, it may hold more of the medicated mass. It is necessary, therefore, to judge the displacement value of the medicament. Thus, in calculating for a 3-gr. tannic acid suppository, it is usual to compute that 2 gr. of tannic acid will displace 1 gr. of theobroma, and therefore each suppository will require 13½ gr. of theobroma. The following have similar

displacement values: alkaloids and alkaloidal salts, dry and soft extracts, iodoform, phenol; whilst liquids and liquid extracts will usually displace their own weight; 5 gr. of a bismuth salt and 3 gr. of lead acetate are reckoned to displace 1 gr. of theobroma respectively.

Preparation of Mould.—Before pouring the melted mass into the mould, the latter must be carefully lubricated, otherwise the suppositories may be difficult to remove. The best general lubricant is a solution of soft soap in alcohol (90 per cent.) with about 20 per cent. of glycerin. It should be applied on a piece of cotton-wool, the inside of the mould being well wetted and rubbed, excess lubricant being finally removed. The mould should then be screwed up and well chilled by being placed in an ice-box or in cold water. If cold water is used it should not be allowed to wet the inside of the mould.

Preparation of Mass.—In preparing the mass, the rules for making an ointment should be followed. If the medicament is soluble in the basis, solution should be effected, and if insoluble, then it should be either very finely powdered and suspended in the basis or dissolved in some other liquid and emulsified (dispersed) in the basis. Soft extract such as Green Extract of Belladonna should be rubbed down to a thin paste with a mixture of glycerin and water, and then thoroughly emulsified in the base. If six suppositories are required, it is usual to make sufficient mass for eight, as a certain loss is unavoidable, chiefly due to the necessity of overfilling the moulds.

The theobroma, which should be powdered or shredded, should be placed in a small evaporating dish and carefully melted on a water-bath, using the minimum amount of heat. About one-half of it should then be poured on to the medicament on a slab and thoroughly mixed. It should then be scraped back into the dish and mixed with the remainder of the melted theobroma, gently warming if necessary. When the mass has been sufficiently softened to pour, the mould should be carefully filled so that each compartment slightly overflows. The mould should then be replaced in the ice-box, and when thoroughly chilled, excess of mass should be sliced off with a knife, the mould opened, and the suppositories carefully removed.

Substances like dry extracts (such as hamamelin, Dry Extract of Belladonna) may be powdered and suspended or treated as Green Extract of Belladonna. Should volatile oils like eucalyptus be prescribed, it may be necessary to incorporate a little white beeswax to produce a hard mass. Substances like phenol and chloral hydrate will cause an appreciable lowering of the melting-point (causing difficulty in setting) of theobroma if mixed at even a moderate temperature. Great care, therefore, should be taken to keep the temperatures of such mixtures at the minimum.

Glycerin Suppositories are made from the mass, the formula and directions of which are given in the Pharmacopœia. Gelatin, cut small, is thoroughly softened in water, excess of the latter drained off, glycerin is added and dissolved on a water-bath, finally making up to weight with water. The mass is moulded in ordinary theobroma moulds, using a trace of almond oil as a lubricant. The following sizes are prescribed: 15 gr. (1 gm.) or Infant's size; 30 gr. (2 gm.) or Children's size; 60 gr. (4 gm.) or Adult's size.

Glycerin suppository mass is generally used when a glycero-gelatin base for a medicated suppository is required. It should be remembered that the mass has a higher specific gravity than theobroma, the relation being approximately $1 : 1{\cdot}2$. Therefore a 15-gr. mould will contain $15 \times 1{\cdot}2 = 18$ gr. of glycerin suppository mass.

Thus for a 3-gr. ichthammol suppository with a glycero-gelatin base, the calculation for one suppository would be as follows:

Weight of theobroma displaced by 3 gr. of ichthammol = 3 gr.

$\therefore$ Weight of glycerin suppository mass $= (15 - 3) \times 1{\cdot}2 = 14{\cdot}4$ gr.

It should be remembered that a glycero-gelatin mass is *incompatible* with drugs containing tannin, which always forms an insoluble compound with gelatin, and therefore suppositories of such drugs should have a theobroma basis.

Pessaries (Pessi) are made in the same manner as suppositories and may be either cone-shaped or of a flat, bi-convex shape. They are of two sizes—60 gr. (4 gm.) or 120 gr. (8 gm.). Unless otherwise specified, the larger size should be made. The basis is either theobroma or glycero-gelatin, the

former being used unless the latter is specified. The student should again remember that a 120-gr. mould is designed to hold 120 gr. of theobroma, and would hold $120 \times 1 \cdot 2 = 144$ gr. of glycerin suppository mass.

Urethral Bougies (Buginaria) are long, thin, medicated pencils having a basis of theobroma or (if specially ordered) a glycero-gelatin base. They are two usual sizes :

(*a*) 15 gr., measuring $2\frac{1}{2}$ inches long.
(*b*) 40 gr., measuring 5 inches long.

They may be prepared by using a special bougie mould, but as the latter are rather expensive and the demand for bougies not common, it is often desirable to make them by an alternative method. The following is recommended : A long glass tube is obtained having a bore the size of a bougie (about $\frac{3}{16}$ inch diameter) and also a piece of glass rod of equal length which can just be passed through the tube. The tube is slightly warmed if necessary, and the mass is sucked up into it. When it has set completely it is carefully pushed out by means of the glass rod and cut up into such lengths as to contain the required weight of medicament. One end can be moulded by the fingers to a blunt point.

CHAPTER X

PLASTERS

Plasters consist of an adhesive base, with or without a medicament, and are intended to be applied to, and to adhere to, the skin, remaining there generally for a considerable period. Unmedicated plasters may be used for drawing the edges of wounds together, for the support of other dressings, or for warmth, whilst the inclusion of a medicament in a plaster base provides a method of keeping it in contact with the skin for a prolonged period and sometimes permitting of slow absorption (belladonna and mercury). Medicated plasters may be either vesicating, stimulating or anodyne in action.

Plaster bases are of three types :

(*a*) Those which require to be softened with heat before application, such as lead and colophony plasters.
(*b*) Those which may be applied without heat, as the heat of the body is sufficient to make them adhere, such as a rubber plaster basis. This consists of a solution of rubber and small quantities of other ingredients in benzene.
(*c*) Those which must be wetted with water in order to make them adhesive, such as court plaster, which has a basis of isinglass.

The material upon which plasters are spread may consist of :

(*a*) Leather, usually white sheepskin. The plaster is spread upon the rough surface.
(*b*) Fabric such as unbleached calico and brown Holland.
(*c*) Swansdown. This is a thick cotton and wool fabric, having a smooth and a rough surface. The plaster is spread upon the smooth surface.
(*d*) Silk. This is used for court plaster.

It is customary to select leather as the material when spreading a plaster on the dispensing counter, unless the prescriber indicates another preference on the prescription. Occasionally a plaster may be required with an adhesive margin, when it is usually spread upon machine-spread lead plaster which has been spread on calico. The latter material is used by most manufacturers in preparing machine-spread plasters, as it is cheaper and more suitable for producing big lengths than leather.

Machine-spread plasters are now in such common use that a short description of their manufacture is called for. The commonest plasters are rubber plasters, court plaster and mustard plaster. Plasters made with a rubber base, unvulcanized rubber, have better adhesive properties than those made with other bases ; they also have a milder action on the skin.

The fabric on which the plaster is to be spread is coated with a rubber solution, rubber mixed with petroleum ether. The rubber plaster base is usually a manufacturing secret, since there is no formula given for it officially. Rubber

adhesive plaster consists of rubber, resins, balsams, wax and lanolin, the active ingredient being mixed in. The rubber is first made into a semi solution in benzene and the resins, wool fat, etc., are melted together, mixed in a special machine, and carried to the " hopper " of the spreading machine. Resins and waxes are not always used, for the active or mineral ingredients, salicylic acid, zinc oxide, etc., may be ground down finely with the lanolin in an ointment mill. Afterwards they are incorporated with the rubber mass, rubber, thinned down with the solvent. Resin usually finds a place in all these rubber plasters, but such substances as dammar, sandarac, copaiba balsam, beeswax and/or olibanum may, or may not, be present.

The manipulation of spreading is fairly simple and consists of :—

1. Hopper to hold the mixed rubber plaster in fluid form, heated by steam or electricity (at the base of this hopper is an adjustable slit which may be any width and, of course, corresponds to the width of the fabric support).

2. A conveyor belt, which unwinds from a drum and just passes below the slit of the hopper, and is carried a certain distance around a larger drum and back at a lower level to a winding drum.

3. At a point before reaching the winding drum, the plaster being now quite dry, a roll of fine gauze unfolds and is carried up against the surface of the plaster by a guide pulley, so that both the plaster and the gauze run together on the winding drum. The layer of rubber plaster on the proofed cloth support is about 1 mm. in thickness, but this can be made thicker or thinner by altering the width of the slit, a fine adjusting arrangement. The secret of success is to get the right temperature and the perfect adjustment of the slit. The spread of the conveyor must also be taken into consideration. The plaster has a definite " run " on the conveyor before it becomes dry enough to be covered with the gauze, and so the temperature must be kept at a fixed point, so that the perfect solidification may be achieved at the point at which the gauze is put on the surface.

Other Plasters.—*Court plaster* is made by coating coloured taffeta with a warm solution of isinglass. Several coatings are given, usually four, and each coat must be perfectly dry before the next one is laid down. Court plaster becomes

adhesive by being moistened in warm water. *Mustard plaster* or "leaves" is made by coating cartridge paper (sometimes cloth) with a mixture of oil-free powdered mustard in a solution of rubber. The powdered mustard is freed from oil by being treated with benzene. The rubber base is dissolved in carbon bisulphide and benzene, and then mixed with the prepared mustard. When the mustard leaves are soaked in warm water, simple moistening is enough, the interaction gives rise to evolution of volatile oil of mustard, useful as a counter irritant when applied to various portions of the body. Machine-spread plasters can be worn by the patient with much more comfort when perforated with small holes, special machinery being employed for making such plasters "porous." Plasters are spread on glazed and unglazed calico, swansdown, brown holland and felt. (From the *Australian Journal of Pharmacy*, April, 1937.)

Blisters.—These are special plasters spread from Cantharidin Plaster and intended to produce a blister on the specified area. Cantharidin Plaster has a basis of a mixture of beeswax, wool fat and castor oil, and is more of the type of a very stiff ointment than a plaster. This is necessary, as on removal of the plaster the blister must not be broken. As the basis itself is not sufficiently adhesive, it is necessary to spread the plaster on some material so as to leave an adhesive margin which will tend to keep the plaster in its correct position. Machine-spread lead plaster is usually employed. The stencil need not be wetted, as it will readily adhere to the lead plaster. As blisters are usually small, they can generally be spread with a small steel spatula.

CHAPTER XI

STERILIZATION

THE development of aseptic surgery, aseptic dressings and the methods of giving medicaments in sterile solution by injection into the blood stream, necessitates a good knowledge

of methods of sterilization by the dispenser, who may at any time be called upon to produce sterile apparatus, dressings or preparations.

The following are some of the terms used in the literature on this subject ; they are given because their meaning is sometimes different from the same words used in medical works.

1. Infection—the transference of a living organism to any preparation or material.
2. Aseptic—applied to any process means that conditions are so arranged that freedom from living organisms is obtained.
3. Sterilization—the killing or removal of living micro-organisms.
4. Sterile preparation—one in which micro-organisms have been killed or removed.

The infection of materials and solutions can occur from varied sources, and a knowledge of such sources is useful in so far as we can then apply logical sterilization processes.

Infection can be :—

(*a*) *Air Borne.*—Normally the air contains dust particles which are a serious and most important source of contamination, not in themselves, but in the fact that micro-organisms are invariably associated with dust particles. The bacterial flora of the air is varied and it is impossible to treat it generally. It is sufficient to say that the air is a source of sporing organisms. Further the air might contain droplets of mucus and saliva from the mouths and throats of people coughing and sneezing. Thus when there is no absolute method of sterilization available, dust particles must be rigidly excluded. When the use of a pressure sterilizer is permitted, the precautions can be relaxed and the preparation is made cleanly and quickly without special aseptic technique, because if sporing organisms are present, they will be killed by the heat and pressure of the steam. It is otherwise when the compound or preparation is such that high temperature sterilization is inadmissible. Then the presence of sporing organisms in the air might lead to contamination of the product, and further, the sterilization process would not be sufficient to kill spores. A case in point is the preparation of vaccines and sera. *General rules of aseptic work* are :

(i) Restrict the number of people working,
(ii) Rigid routine and technique,
(iii) Filter the air entering the room free from dust particles,
(iv) Further various special methods are used to free the room from dust particles; positive pressure of air in the room, that is, all the air that is pumped into the room, is filtered; the use of steam to carry down any dust particles present, etc.

(*b*) *From Contact* with hands, containers, etc. Hand contamination is probably the most important. Even if the hands are scrubbed well with soap and water and the surface treated with disinfectant, the problem is not solved, for the first drop of sweat from the glands would carry up and flood the surface of the hand with organisms. The problem is not so important for us as for surgeons, as the organisms are usually staphylococci which are non-sporing organisms killed at 60° C. The contamination from the containers is avoided by using sterile apparatus. This is easily done and is convenient as sterile vaccine bottles, ampoules, jars and flasks can be stored in an aseptic manner, ready for use.

(*c*) *From the Medicament.*—Medicaments for use in injection should be kept apart from the usual stock. The bottles should be either screw cap wide mouth, or special glass stoppered with protecting dust cap ridge. The ordinary "shop round" is not good as dust collects round the lip and falls in every time the stopper is removed. This method of storing medicaments does not deal with the primary problem, the state of the medicament as it arrives from the manufacturers. The most that can be asked at the present time is that the medicament be reasonably clean. In general most pure chemicals of the nature of sodium chloride, dextrose, lactose, etc., satisfy this criterion. Indeed, out of twenty separate samples of sodium chloride and dextrose, which were tested for sterility, eighteen were proved sterile. On the other hand, twenty out of twenty samples of powdered acacia were very heavily contaminated. This indicates the general conditions, namely that pure chemicals are usually received in a clean condition and that powdered drugs cannot be expected to be free from contamination.

Thus the most important sources of infection are from the air and from the medicament. Both of these are liable to contaminate the product with spores. Careful technique

can minimize the aerial contamination and this should be done when the sterilization process is not sufficient to kill spores, or when no final sterilization process is applied.

Now having discussed the sources of contamination, it is necessary to draw attention to those conditions that help to destroy bacteria. The most important is the effect of temperature. The optimum temperatures for bacterial growth are:

Most pathogenic organisms	37° C.
Other organisms vary	20–43° C.
Saprophytic organisms and moulds . .	20–25° C.

Extremes of cold do not in general kill bacteria, but merely inhibit growth. The growth rate for the majority of organisms falls rapidly above 40° C. and ceases at about 45° C. Certain thermophylic organisms can multiply freely at 60–70° C. Thus we speak of the Thermal Death Point of a species, the minimum temperature that will kill. It varies considerably according to other factors, i.e. whether dry or moist heat is used (hot air or steam). Another important factor is that of time, for the organism will not die instantaneously unless a high temperature is used. This cannot be done with many medicaments. Then with lower temperatures the process of killing is gradual and thus a heavy infection is likely to take longer to destroy than a small infection. Further, other conditions such as the hydrogen ion concentration, affect the Thermal Death Point. For a generalization we can take the Thermal Death Points and times as:

(*a*) Wet Heat.
 Vegetative organisms—60° C. for 1 hour.
 Spores—may not be killed even at 100° C. for several hours. 115° C. for half an hour ensures sterility.

(*b*) Dry Heat.
 Vegetative organisms easily killed.
 Spores—150° C. for 1 hour.

Another condition which can be made unfavourable to bacteria is the hydrogen ion concentration—the degree of acidity or alkalinity of a solution. This is denoted by the symbol *p*H. Neutrality is taken as near *p*H 7·0; numbers smaller than this indicate an acid solution (N/10 hydrochloric acid has a *p*H near 1·0; N/100 near 2·0 and so on); numbers

larger than 7·0 indicate an alkaline solution. For most bacteria the optimum *p*H is from 7·2–7·8, slightly alkaline. The range of *p*H in which bacteria can grow is approximately from *p*H5–*p*H9, outside this growth ceases and the organisms gradually die. Many pharmaceutical solutions have a *p*H well outside the optimum range for bacteria :

Insulin solution . .	*p*H 3–4
Liquid Extract of Pituitary	*p*H 3–4
Solution of Adrenalin .	*p*H 2·6

These solutions of themselves inhibit bacterial growth. Moulds can grow at degrees of acidity far beyond those in which bacteria can grow. Even so, for many pharmaceutical solutions we can reasonably assume that the T.D.P. is reduced. Here is a list of some solutions for injection with their approximate *p*H.

Morphine hydrochloride 2·5% .	*p*H 4·9
Strychnine hydrochloride 1·0% .	*p*H 6·0
Atropine sulphate 0·12% . .	*p*H 6·6
Codeine phosphate 5·0% . .	*p*H 4·8
Caffeine and sodium benzoate 10%	*p*H 9·2
Homatropine hydrobromide 0·6%	*p*H 4·8
Pilocarpine nitrate 3·0% . .	*p*H 4·6
Hexamine 20%	*p*H 9·2
Novocaine 2·0%	*p*H 5·3
Phenobarbitone soluble 10% .	*p*H 9·4

The use of chemical disinfectants is limited since only such solutions can be used as have no harmful effects on the patient when injected. Thus we are of necessity restricted to using antiseptics in dilute solution, and in general these weak solutions have bacteriostatic action only. That is, they prevent the development of bacteria. If contamination occurs, then no growth is possible and the contamination remains small. They have, it is true, a bactericidal value, but this is low, i.e. the power of killing is slow.

The two latter phenomena, *p*H and bacteriostatic value, acting together, must in many pharmaceutical solutions inhibit growth considerably and reduce the T.D.P.

Sterilization Processes.—The processes can be divided into two classes :

A. Absolute Methods.

These methods do not require special aseptic technique. There is no need to sterilize any of the apparatus used in making the solutions.

(i) *Dry Heat.*—Dry heat at 150° C. for one hour is an absolute method for the sterilization of oils and glass ware. The temperature is usually obtained by means of an *oven*, which can either be heated by gas or electricity. Electric ovens take a long while to heat up and to cool down. Gas

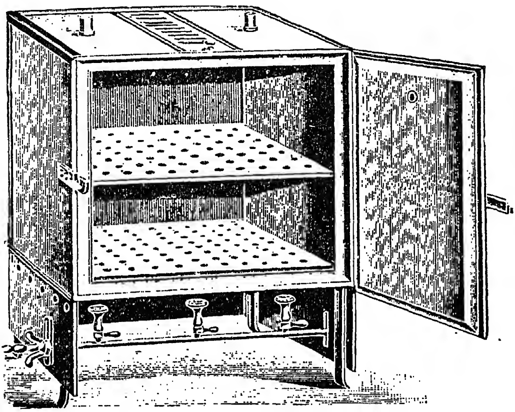


FIG. 20.—Hot-air oven.

heated ovens are simpler and quicker. It is important that the real temperature of the apparatus or oil is 150° C. and not that the thermometer at the top of the oven reads 150° C. Thus for oils, the thermometer should dip into a bottle of oil which is placed in the oven at the same time and on the same shelf as the oil to be sterilized. The time should be reckoned as beginning when the thermometer reads 150° C. Further it is wise not to place the bottles on the bottom, since the temperature may be considerably more than that registered at the top of the oven. This avoids overheating and discolouration.

Oils may be sterilized in plugged, stoppered or screw-capped bottles or in ampoules. In the preparation of oculenta the base (90 per cent. yellow soft paraffin, 10 per cent. wool fat) can be sterilized in a porcelain basin covered with a Petri dish, since it has to be subsequently triturated with the medicament. It is a general rule that oils and paraffin mixtures should be filtered before use. This should be done in the oven as the process of filtration is hastened considerably. Special oil filtering paper increases the speed of Filtration (Postlip mills No. 663 is efficient).

Glassware is conveniently sterilized in a *hot-air oven*. Thick glass ware—mortars—should be treated with care and heated slowly to 150° C. and not removed from the oven until reasonably cold. Pipettes and bottles can be sterilized in this way. No apparatus with rubber fittings can be sterilized in the hot air oven. Autoclaving and subsequent drying at 70–80° C. is the rule. Powdered kaolin and other heat stable substances can be sterilized by heating at 150° for one hour in a thin layer.

(ii) *Wet Heat*.—The Autoclave. An absolute method in general use for the sterilization of solutions is to heat the solution in an *autoclave* for half an hour at a pressure of 10 lbs. in excess of that of the atmosphere. This corresponds to a temperature of 115·6° C. provided conditions for saturated steam obtain. An autoclave is essentially a pressure boiler, fitted with a pressure gauge; from this pressure the temperature is inferred. For this to be true, i.e. the theoretical relationship between pressure and temperature, the atmosphere in the autoclave must be entirely of steam with no air admixture. This condition is reached in practice by allowing the steam and air to escape from a stopcock until it is deemed all the air is removed. Then the following table gives the correction between the pressure registered by the gauge and the temperature inside the autoclave.

PRESSURE ON THE GAUGE.	TEMPERATURE OF STEAM.
5 lbs.	108·8° C.
10 lbs.	115·6° C.
15 lbs.	121·3° C.
20 lbs.	126·2° C.
30 lbs.	134·6° C.

When a larger bulk of liquid is heated in an autoclave, it

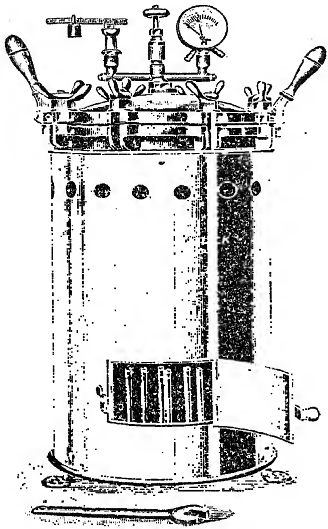


FIG. 21.—Autoclave.

takes some time for the temperature of the liquid to rise to that of the autoclave. The Pharmacopœia, recognizing this fact, specifies the following times for different bulks of solution.

For liquids of 100 millilitres or less—10 lbs. in excess of atmospheric pressure for 30 minutes.
For liquids of 250 millilitres—10 lbs. in excess of atmospheric pressure for 45 minutes.
For liquids of 500 millilitres—10 lbs. in excess of atmospheric pressure for 50 minutes.
For liquids of 1,000 millilitres—10 lbs. in excess of atmospheric pressure for 55 minutes.

The most important practical points concerning the use of the autoclave are :

1. Sufficient water must be added to provide excess.
2. Allow the steam to issue for some time before closing the stopcock.
3. Regulate the heat supply until the desired pressure is produced and time the process from this moment.
4. After the requisite period has elapsed, turn off the heat and allow the pressure indicator to return to zero. Then open the steam cock and admit air slowly.
5. If possible allow the material to cool in the autoclave.

N.B.—The autoclave is only efficient if wet heat is used. If an oil is enclosed in an ampoule then it cannot be sterilized by 10 lbs. pressure heating in an autoclave, since the process is obviously one of dry heat at 115·6° C. and this is not an absolute method.

(iii) *Wet Heat*.—" Heating with a Bactericide." This process has been made official by the Fourth Addendum (1941) and replaces the " Emergency Process " of the Pharmacopœia (1932). The solution is made without aseptic technique and 0·2% w/v para-chlor-meta-cresol (Chlorocresol, B.P.) or 0·002% w/v phenylmercuric nitrate, is incorporated. The finished solution is placed in its final container and subjected to a temperature of 98° C. for 30 minutes by immersing the container in flowing steam. If the volume in the container is more than 30 mils the time must be increased to ensure that the whole of the contents are at 98° C. for 30 minutes. Intravenous injections, which have a dose of more than 15 mils, must not be prepared by this method, because the bactericides would be toxic if larger doses were given. This method cannot be used for intratracheal or intracisternal injections.

Although this process has only recently been made official, it has been used for many years by pharmacists, the bactericide being 0·5% w/v phenol. There is no doubt that 0·2% para-chlor-meta-cresol is more active as a bactericide than 0·5% phenol, and this fact renders a greater margin of safety possible by the new method. The process is, in fact, considered absolute, as no tests for sterility are required, and no aseptic technique demanded in the preparation of the solution. The Fourth Addendum (1941) uses this method for such medicaments that are not stable to the temperature of the autoclave (115·6° C.). A list of suitable methods for sterilizing solutions is given later (page 222).

B. Methods which are Not considered Absolute for Pharmaceutical Solutions.

(i) *Tyndallization.*—The process is based on a discovery by Tyndall that certain nutrient media, even when contaminated with sporing organisms, could be sterilized by heating at a temperature below boiling point, if the process was repeated on successive days. Spores can, of course, withstand boiling water for long periods, but if the process is made discontinuous, the spores germinate in the periods between the heatings, and the vegetative organisms are killed by the next heating period. The method has been used with success for the sterilization of culture media, but the process has been deleted by the Fourth Addendum (1941) and is not now official for the sterilization of pharmaceutical solutions. Pharmaceutical solutions often do not permit the germination of the spores in the periods between the heatings and therefore the process is not reliable if spores are present. This process is replaced by the process of "heating with a bactericide."

(ii) *The "Emergency Method of Sterilization."*—This process was official in the Pharmacopœia but was deleted in the Fourth Addendum (1941). The method was to prepare the solution using aseptic technique, incorporate 0·5% w/v phenol, seal in the final container and subject to a heating process of 80° C. for 30 minutes. For intravenous injection, the phenol was omitted, and the solution was boiled for 15 minutes.

Here follows a résumé of some of the more important temperatures connected with sterilizing processes.

0–10° C.	most bacteria can survive for long periods (without multiplication)
15–20° C.	average room temperature
22° C.	optimum for moulds
37° C.	blood heat, optimum for pathogenic organisms
42–45° C.	enzyme optimum
56° C.	highest temperature to which blood serum can be heated without destruction
98° C.	Official process, "heating with a bactericide."
115° C.	Autoclave; official B.P. temperature T.D.P. for all forms if wet heat used.
150° C.	Hot-air oven; official B.P. temperature for dry heat T.D.P. for all forms when dry heat is used.
160° C.	Above this temperature cotton-wool chars.

(iii) *Filtration*.—Filtration is classed with those processes needing aseptic technique, because although all bacteria are filtered from the solution, the problem is to place a sterile solution into its final container without contamination. Thus the process is not absolute in the sense that the solution is sterilized in its final container. There is no heat process in the official method. The solution must comply with the official tests for sterility. Many varieties of material are used for filtering—Kieselguhr, Kaolin, porcelain, or asbestos. The pores of the filter are often larger than bacteria and filtration is a complex phenomenon and not a simple sieve-like action. Rate of filtration depends on many factors of which the viscosity and *p*H of the solution are two. These factors for a particular solution are constant and another important point is the pore density of the filter. Now to increase the rate of filtration we cannot increase the size of the pores too much, but with certain porcelain filters it is possible to vary the number of pores per unit area. When this is high then the rate of filtration is higher than when there are few pores per unit area.

Filters of the candle type should be tested before use. A rough and good test is to immerse the candle in water and push air through, when it should stand a pressure of 8 lbs. per square inch without letting air pass. When bubbles of air are formed, they should be uniform and small in size; if there is a pin hole in the filter a stream of larger bubbles emerges from this point and the defect is easily noticed. Filters can also be tested with a living organism. For this purpose *Chromobacterium prodigiosum* is used. It is a small coccus and has the ability to develop a red pigment if exposed to diffuse light. Thus if a suspension of this organism is made in nutrient broth, filtered and the filtrate incubated, the development of a red pigment indicates the filter is not efficient in removing organisms. It should be discarded.

Another factor to be considered is the absorption of the medicament by the filtering material. This is probably not important when large quantities are filtered. For small quantities it is a variable factor and for each solution and each filtering medium different factors can be obtained. It is wise then, in dealing with small quantities, to neglect the first portion of the filtrate.

Types of Filters.—(*a*) The *Berkefeld Filter* is made of

kieselguhr, usually in the form of a candle with a metal top. The solution is sucked through the filter into a sterile reservoir. The Berkefeld filter is made in three grades.

V—coarsest
N—intermediate
W—finest

The W type is usually employed and should hold back *Chromobacterium prodigiosum*. The N type has been used if a "bed" is built up in its pores and the first portion of the filtrate discarded.

(*b*) The *Mandler Filter* is similar to the Berkefeld, but is made in U.S.A. It is very reliable.

(*c*) The *Chamberland Filter* is made of unglazed porcelain. It also is made in many grades, of which the following are the more important:

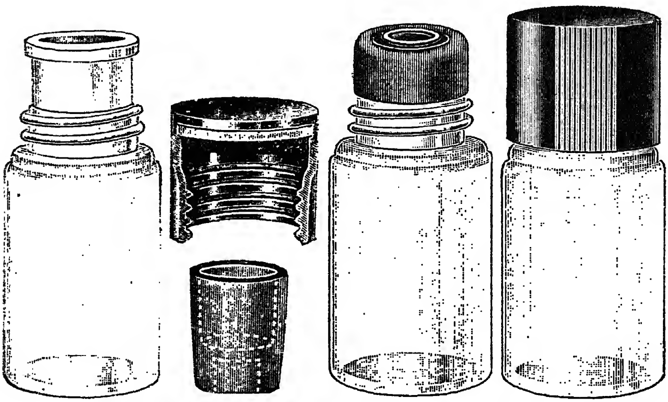
L_1	a clarifying filter	— Berkefeld V
L_2		— Berkefeld N
L_3		— Berkefeld W

(*d*) *Doulton Filters* are accurate British filters of porous porcelain. A type to be recommended for small quantities is the Guy's Hospital pattern. This has a rapid rate of flow and is reliable.

All the above filters when fitted up to the reservoir for receiving the sterile filtrate can be sterilized in the autoclave. Practical points concerning the handling of filtration apparatus can only properly be appreciated by experience.

Containers for Sterile Preparations.—Containers may be either for a single dose or for a multiple dose. The former are to be preferred as infection might occur when the latter are used and successive doses are withdrawn. The ampoule is the commonest single dose container and is common in sizes from 1 mil to 100 mils. The glass should be of good quality and free from alkali. When filling ampoules more than the required dose should be inserted, i.e. 1·1 mil when the dose is 1·0 mil, to allow for easy withdrawal by the syringe. Some varieties of glass flake on autoclaving and batches should be examined carefully in a good light for glass particles. For quantities over 100 mils either a plugged flask, a milk bottle or a screw capped bottle can be used. The latter can be obtained in a variety of sizes and with screw necks of such sizes

that special fittings for intravenous use can be obtained (Gallenkamp). For multiple doses the vaccine bottle fitted with rubber cap is the only container in general use. The cap is important. Black caps are in general cold cured, i.e. dipped in rubber solution. The process is repeated several times so that layers of rubber are built up. The rubber often contains air bubbles and its tensile strength is poor. It will only stand one autoclaving. Red caps are usually heat vulcanized



Assembly Details. I.R. Cap Fitted. Completed.

FIG. 22.

and made in a mould. They are stronger and better altogether. Both these caps cannot be wired on before autoclaving as they will then rupture. They have to be autoclaved with an air vent and this subsequently closed after the process is finished. This is an unsatisfactory process ; to overcome this disadvantage a skirted cap, which will stand autoclaving, has been elaborated. It is now available fitted to a special alkali-free glass bottle (Fig. 22). The cap is not wired on but is kept in position by a bakelite screw cap, which entirely covers the rubber cap. Inside the bakelite cap is a pad on which is to be dropped an antiseptic solution. Thus the problem of

keeping the surface of the cap clean has been solved and the problem of rendering it sterile has been approached.

When a dose is removed from the vaccine bottle then a hole is made in the cap. When new the rubber of the cap closes the hole; when old, the holes open. It is thus obviously better if the top of the cap is not under tension but under compression. The latter condition holds for the new skirted cap and the former for the ordinary red or black vaccine cap. The practice of putting a layer of wax over the surface of the cap is to be deplored as it would almost certainly result in the needle becoming clogged. It is obvious that a vaccine bottle containing sufficient solution for 25 doses must be treated carefully if the contents are to be sterile when the bottle is nearly empty. If the surface of the cap is wiped with a disinfectant and the needle sterilized before insertion, this condition is more likely to be obtained.

The Quality of the Glass.—As far as pharmaceutical work is concerned the quality of the glass is important in so far as determining whether substances are dissolved from the glass during storage. One consideration is the glass making the solution more alkaline. Many pharmaceutical solutions are more stable in acid than in alkaline solutions:

(*a*) Adrenaline salts. The official solution of adrenaline hydrochloride is acid (*circa* *p*H 3). At this *p*H it is relatively stable. At a more alkaline *p*H it is more susceptible to oxidation. As the adrenaline decomposes, the solution turns pink, then red and finally brown and forms a precipitate.

(*b*) Apomorphine salts in an alkaline solution quickly turn green.

(*c*) Morphine salts turn yellow in alkaline solution.

(*d*) Physostigmine rapidly oxidizes and turns red in alkaline solution.

(*e*) Insulin is unstable in alkaline solution.

(*f*) The official Pituitary injection (Extract of Pituitary) is adjusted to a *p*H of between 3 and 4. 10 to 20 per cent. of the oxytocic activity is lost during sterilization at *p*H 3–4. 50 per cent. of the oxytocic activity is lost during sterilization at *p*H 5.

All the above examples are arguments for the use of glass which does not yield alkali to a solution. Recognizing this, the Pharmacopœia has prescribed a test for the alkalinity of

glass. There is a test on whole and one on crushed ampoules. The latter is probably too severe since many manufacturers put a resistant film on their glass so that the ampoules would pass the whole ampoule test but possibly fail on the crushed glass test. For details of the test refer to the B.P.

The Colour of the Glass.—Many pharmaceutical solutions are unstable to light. Coloured glass ampoules and vaccine bottles are used to minimize actinic effects. The practical point is that the ampoules are kept in boxes and the vaccine bottles in boxes or cupboards so that the effect of light is minimized.

The Dispensing of Parenteral Injections.

The following general rules are described in the Fourth Addendum (1941)—

1. When the container is sealed so as to permit the withdrawal of successive doses (e.g. a vaccine bottle, sealed with a rubber cap) the solution contains a suitable bacteriostatic agent in such concentration as will prevent the growth of micro-organisms. Phenol 0·5% w/v, and para-chlor-meta-cresol 0·1% w/v have been used; the latter is the more efficient solution.

2. Rubber caps for vaccine bottles are made from a good quality heat-vulcanized rubber. Before use they are boiled in several changes of water and then either stored or boiled for 30 minutes in a solution containing the bacteriostatic agent, in the same concentration that is used in preparing the solution.

3. Solutions for intrathecal or intracisternal injection are only dispensed in single-dose containers.

Details of the Preparation of Sterile Solutions.—Whilst some methods of preparation call for greater aseptic technique and skill than others, it is a general rule that all operations connected with sterilization should be done in a clean manner. This is important even for the absolute methods, as otherwise the solution might contain considerable numbers of bacteria, which although dead, are undesirable in any solution for injection.

Thus a special room for sterilization processes should be used if possible. This room should be designed so that it is readily cleaned. It should contain autoclave, hot air oven

and drugs. These drugs should be kept apart from the normal "pharmaceutical drugs" in bottles fitted with dust-cap stoppers. A constant supply of freshly distilled water is available. Measures, filtering apparatus and containers should be kept clean and wrapped or capped with paper. Ideally the air should be filtered and pumped into the room so that a positive pressure exists inside. Clean white overalls should be worn and kept in the laboratory. The hands should be well washed and scrubbed.

The procedure adopted will vary with the stability of the medicament and the type of container. Here are some typical examples.

1. *To prepare 1 litre of Normal Saline B.P. for intravenous injection.*

Wash measures, filters and container well with tap water. Make a 0·9 per cent. solution of sodium chloride in freshly distilled water. Filter through the washed sintered glass filter (size 17 G 3 is suitable for a litre) into the container. Use either a milk bottle, screw-cap bottle or plugged flask as a container. Autoclave at 10 lbs. pressure in excess of atmosphere for 50 minutes. Allow to cool in the autoclave. Remove and affix appropriate label. A strip label should be placed over the container stopper giving the date and bearing the word "Sterilized." If a flask is used, the plug should be of non-absorbent wool, wrapped in muslin. After autoclaving, cover the plug with cellophane, and affix a "sterilized" strip label.

Sintered Glass Filters.—Sintered glass filters are made of small particles of glass cemented together by "sintering" the powdered glass at a particular temperature. Their advantage is that when properly used they yield no fibres to the solution passing through. They stand steaming and autoclaving, but care should be taken not to expose them to sudden temperature changes. A variety of sizes and fineness of pore is available :—

Numbers 1 *and* 2 are coarse filters.

Number 3—a finer filter suitable for injections. Nos. 1, 2 and 3 can be used without reduced pressure; filter by gravity alone, although No. 3 is rather slow.

Number 4—still finer; requires reduced pressure to suck the solution through.

Number 5 on 3—this has the finest pore. It will remove bacteria and can be used instead of the Doulton, Chamberland or Candles.

For general use a No. 3 is used. Sizes vary; for quantities of about 50 mils, 3 G 3; for quantities of over 100 mil 17 G 3. Larger ones are available. The filter must be kept clean. After use each filter should be cleaned by forcing water through in the opposite way to which the solution ran when filtered. This can be simply done by attaching the stem of the filter to a rubber tube and thence to the tap. Periodically the filters require energetic cleaning. This is done by pouring on to the surface of the filter strong sulphuric acid to which has been added a few crystals of sodium nitrate. Allow to drip through slowly, often takes overnight. Then well wash in tap water until no acid remains. Unless kept clean and treated with care, sintered glass filters will yield indifferent results.

2. ℞.

Morphinæ Hydrochloridi 2·5 per cent.

Ft. solutio. Sig. 0·5 mil *pro dosi.*

Proceed as before and make sufficient 2·5 per cent. morphine hydrochloride solution. Filter into a well-washed bottle. Affix the vaccine cap which has been well boiled in water. This is primarily to clean it. If a black or red rubber cap that will not stand autoclaving is used, make an air vent between the cap and the bottle so that the cap will not burst. This is usually done with a piece of wire. Autoclave at 10 lbs. pressure in excess of atmosphere for ½ hour. Cool in autoclave, remove wire and wire the cap on. Affix appropriate labels. This type of solution has usually to be sent out to a ward, or to a doctor, thus:

Solution of Morphine Hydrochloride, 2·5 per cent.
Dose—0·5 mil ≡ 0·0125 G. (1/5 gr.)
Sterilized and the Date.
Contains 0·5 % phenol.

3. ℞.

Strychnin. Hydrochlorid. gr. 1/30.
Aquam ad. ♏ x.

Ft. solutio pro injectio. Pone in ampulla. Mitte x.

Strychnine hydrochloride will stand autoclaving. Thus no particular aseptic technique is needed. Well wash measures.

and syringe. The syringe can be fitted with a long needle or a cannula, the latter allowing for quicker filling. The ampoules are received from the manufacturers sealed. File and break off all the ampoules so that the lengths of neck are the same and so that they will fit the ampoule bore. Make sure no pieces of glass fall into the body of the ampoule. It is wise to tap the ampoule, open end downwards, on a porcelain tile to dislodge any glass particles inside. The ampoules may require washing. Weigh one grain of strychnine hydrocloride on a chemical balance and dissolve in sufficient water to produce 300 minims. Filter through sintered glass, fill 11 minims into each of the ampoules and seal. Ampoule sealing bunsens are available. *Meker* burners give a very hot flame and are suitable. Test for sealing by immersing the ampoules neck downwards in hot methylene blue solutions and cool with the ends still below the surface. Examine over a white surface and reject any coloured ampoules. It is wise to examine for sealing before autoclaving. The test can be done by immersing the ampoules neck downwards in methylene blue solution and placing in the autoclave. When the process has finished cool as before and reject coloured ampoules; if the test is made before autoclaving, then one is sure that all the ampoules placed in the autoclave are sealed. If it is done in the process then the number of sealed ampoules is not known until the end of the process. This should not affect an experienced worker as the hand sealing of ampoules is a relatively easy matter. It might affect a student! Label the ampoule box:

Ampoules of Strychnine Hydrochloride Solution.
Each ampoule contains 10 minims $\equiv \frac{1}{30}$ gr. strychnine hydrochloride.
"Sterilized"; and the Date.

The individual ampoules should be labelled:

10 minims $\equiv \frac{1}{30}$ gr. Strych. Hydrochlor.

4. ℞.
Hyoscin. hydrobrom. gr. $\frac{1}{100}$.
Aquam ad. ♏ x.

Ft. solutio pro injectio hypodermica. Mitte xii. *Sig.* min. x. *pro dosi.*

Hyoscine hydrobromide is a substance which will not stand

the temperature of the autoclave (115·6° C.). The Pharmacopœia considers that it will not be decomposed at a temperature of 98° C. for 30 minutes. Hence the process of "heating with a bactericide" can be used. No aseptic technique is required. Make an 0·2% solution of para-chlor-meta-cresol in freshly distilled water and use this to make the hyoscine hydrobromide solution. 1 grain of hyoscine hydrobromide dissolved in 1,000 minims of 0·2% para-chlor-meta-cresol will give a solution of the required strength.

Fill the ampoules with 11 minims of this solution, seal, test for sealing, place in a steamer and expose to steam for 30 minutes.

Label:

Ampoules of Hyoscine Hydrobromide Solution.
10 minims is equivalent to $\frac{1}{100}$ gr. Hyoscine Hydrobromide, in 0·2% para-chlor-meta-cresol.
Sterilized :—(Date).

Sterilization of Oily Solutions.—A solution or suspension in oil is directed to be sterilized by heating to 150° for one hour. If, however, this temperature would cause a chemical or physical change, the solution or suspension is directed to be prepared by aseptic methods, and oil which has previously been heated to 150° for one hour is used. The following official injections are sterilized by this method: Inj. Bism. Salicyl., Inj. Hydrarg., Inj. Hydrarg. Subchlor. The temperature is usually obtained by using a hot-air oven.

THE INFLUENCE OF STABILITY OF MEDICAMENT ON THE CHOICE OF STERILIZATION METHOD

The following table illustrates how methods of heat sterilization are affected by the thermo-stability of the drug.

Methods of sterilization				
For oily injections		For aqueous injections		
If medicament stable at 150° C. for 1 hour.	If medicament not stable at 150° C. for 1 hour.	If medicament stable at 115°–116° C.	If medicament stable at 98° C. but not at 115° C.	If medicament unstable at 98° C.
Dissolve or suspend in oil, and heat so that whole of the contents are at 150° C. for 1 hour. (Absolute process.)	Sterilize oil separately at 150° C. for 1 hour. Incorporate medicament, using aseptic precautions, transfer to sterile containers, seal. (Not an absolute process.)	Autoclave, 30 min., 115°–116° C., in saturated steam. (Absolute process.)	Heat at 98° C. with a bactericide. (Considered an absolute process.)	Dissolve in sterile water immediately before use. (Not absolute.) Or filter through bacteriological filter (see page 218).

SUMMARY OF THE OFFICIAL METHODS OF STERILIZATION INVOLVING HEAT PROCESSES

In the preceding pages, the official methods of sterilization have been described, but in view of the many recent changes in these methods, a summary is given below of the additions and deletions of the First (1936) and Fourth (1941) Addenda, together with notes explaining points of importance.

PROCESS.	1932 PHARMACOPŒIA.	1936 ADDENDUM I.	1941 ADDENDUM IV.	NOTES.
1. Sterilization of glass vessels and containers.	Heat to 150° C. for 60 min., or heat in autoclave.	No change.	Free apparatus from grease, heat at not lower than 150° C. for 60 min., or expose to saturated steam at 115°–116° C. for 30 min.	—
2. Heating in an autoclave.	Distribute solution in final containers and seal. When volume is not more than 100 c.c., expose to steam at 115°–116° C. for 30 min. This temperature is reached when pressure of steam is 10 lb. in excess of atmospheric pressure. Increase time, if volume of solution is more than 100 c.c.	No change.	As B.P. 1932, but deletes reference to the pressure of steam. States conditions as in saturated steam at 115°–116° C. for 30 min.	10 lb. excess pressure on steam will only correspond with 115°–116° C. if the steam is saturated (not mixed with air), hence the deletion of pressure (1941) and substitution of temperature.
3. Tyndallization.	Distribute solution in final container, seal, and heat at 80° C. for 60 min., on three successive days.	Added—aseptic methods used in the preparation of the solution.	Deleted the process.	The process is unreliable for the sterilization of pharmaceutical solutions, as spores do not necessarily germinate in the intervals between successive heatings.

4. Heating with a bactericide.	—	—	Introduced in 1941. Prepare solution in 0·2% p-chlor-m-cresol, or 0·002% phenylmercuric nitrate. Use *no* special aseptic precautions. Distribute solution into final containers, seal and heat at 98° C. (steam) for 30 min. Increase time if volume greater than 30 c.c. *Not* to be used for intravenous injections, if dose is greater than 15 c.c. and *not* to be used for intrathecal or intracisternal injections.	Process considered absolute, hence no aseptic precautions necessary. Cannot be used for large-volume intravenous injection, because the dose of bactericide would be too large.
5. Sterilization of oily solutions and suspensions.	Sterilize at 150° C. for 60 min. If ingredients destroyed at this temperature, sterilize oil separately at 150° C. for 60 min., and incorporate medicaments with aseptic precautions. In either case transfer to sterile containers and seal. No final sterilization.	No change.	As B.P. 1932, but adds—if volume greater than 30 c.c., increase time of heating.	If all materials thermostable, the method is absolute. If not, organisms may enter during aseptic process of incorporating materials with sterile oil.
6. The "Emergency Method."	Prepare solution using aseptic technique. Add antiseptic equivalent to 0·5% phenol. Distribute into sterile containers, seal, heat to 80° C. for 30 min. Label—"Keep in a cool place and use within four days." If for intravenous use, omit phenol, prepare by aseptic methods and boil for 15 min.	No change.	Process deleted.	This process was not considered absolute, hence the label, which prevented growth of organisms in the solution before use. Deleted 1941, because heating with bactericide a more efficient process.

METHODS OFFICIALLY SANCTIONED FOR THE STERILIZATION OF SOLUTIONS

The Fourth Addendum (1941) gives a list of methods of sterilization chosen for different substances. This list replaces any directions for sterilization given in the Pharmacopœia (1932) and in the First Addendum (1936). A similar list appears below, with added notes.

DRUG.	AUTO-CLAVING.	HEATING WITH BACTERICIDE.	FILTRATION.	SPECIAL METHODS AND NOTES.
Amylocain. Hydrochlor.	−	+	+	Use alkali-free containers.
Antimon. et Potass. Tart.	+	−	+	*
Antimon. et Sodii Tart.	+	−	+	*
Apomorphin. Hydrochlor.	−	+	+	Incorporate 0·05% sodium metabisulphite in solutions. Decomposition may occur on keeping, with increase in toxicity. Green solutions should be neglected. Use alkali-free containers.
Atropin. Sulphas.	−	+	+	Use alkali-free containers.
Barbiton. Solubile. ..	−	−	−	Dissolve in sterile water, immediately before use.
Bismuthi et Sod. Tartras.	+	−	+	*
Caffein. et Sod. Benz. ..	+	−	+	*
Calc. Chlor. Hydratum.	+	−	+	*
Camphora	−	−	−	Oily solutions sterilized by heating in sealed containers at 150° C. for 60 min., or dissolve camphor in sterile oil.
Carbacholum	+	−	+	*
Cocain. Hydrochlor. ..	−	+	+	*
Dextrosum	+	−	+	Solutions may darken on autoclaving, especially if alkaline.
Diamorph. Hydrochlor.	−	+	+	*
Digoxinum	+	−	−	Use 70% alcohol as solvent.
Emetin. Hydrochlor. ..	−	+	+	*
Ergotoxin. Ethansulph...	−	−	−	Dissolve in sterile water, immediately before use. Use alkali-free containers.

DRUG.	AUTO-CLAVING.	HEATING WITH BACTERICIDE.	FILTRATION.	SPECIAL METHODS AND NOTES.
Hexamina	+	−	+	After autoclaving, the sealed container must not be opened until at least 2 hours have elapsed after cooling to room temperature.
Hexobarb. Solub.	−	−	−	Dissolve in sterile water, immediately before use.
Histamin. Acid. Phosph.	+	−	+	Use alkali-free containers.
Homatropin. Hydrobrom.	−	+	+	Use alkali-free containers.
Hyoscin. Hydrobrom. ..	−	+	+	Use alkali-free containers.
Indicarmin	+	−	+	Protect solution from light.
Iodophthalein	−	−	+	Also by dissolving in sterile water immediately before use. Use alkali-free containers.
Iodoxylum	−	−	+	Also by dissolving in sterile water immediately before use.
Morphin. Hydrochlor. ..	−	+	+	Use alkali-free containers.
Morphin. Sulph.	−	+	+	Use alkali-free containers.
Morphin. Tart...	−	+	+	Use alkali-free containers.
Neoarsphenamin	−	−	−	Dissolve contents of sealed ampoule in sterile water. Solutions rapidly decompose, use within 5 min.
Nikethamidum	+	−	+	*
Ol. Hydnocarp. Ethylic.	−	−	−	Heat at 150° C. for period which ensures whole of contents are at that temperature for 60 min.
Phenobarbit. Solub. ..	−	−	−	Dissolve in sterile water, immediately before use.
Physostigmin. Salicyl. ..	−	+	+	Use freshly boiled and cooled distilled water, and alkali-free containers.

ation. There is a standard time for the first appearance of the dye in the urine and also a time for total excretion.

5. *Methylene Blue* is used in the same way.

6. *Uroselectan* is used for X-ray examination of kidneys and urinary tract.

Requirements for injections:

1. *Sterility.*

2. *Tonicity.*—Another important consideration is the osmotic pressure exerted by solutions when injected. The blood consists of a clear fluid, the blood plasma, which has, suspended in it, large numbers of red blood corpuscles, each of which contains a fluid. If a solution be injected into the blood-stream of a different osmotic pressure to the fluid in the corpuscles, the latter will either collapse or swell up and possibly burst. This may lead to serious results. Consequently it is advisable that an injection shall have the same osmotic pressure as blood plasma, or, as it is termed, the two shall be isotonic.

For intravenous injections isotonicity with the blood plasma is advisable. For hypodermic injections, it is not usually necessary. A solution of sodium chloride containing 0·9 per cent. NaCl w/v is isotonic with blood plasma.

Methods of calculation of the percentage strength of solutions isotonic with blood plasma:

Methods of Calculating Isotonic Strengths.—From the experimental fact that blood serum has an osmotic pressure of 6·7 atmospheres at 0° C. it can be calculated

(*a*) For a non-ionizing substance, the percentage strength for isotonicity is 0·029 Molar. Hence multiply the molecular weight of the substance by 0·029 and the result is the percentage strength of the isotonic solution.

Thus to prepare a litre of isotonic glucose solution—

Molecular weight of glucose = 180 × 0·029

Percentage strength for isotonicity = 5·22 per cent.

Therefore 52·2 gm. of glucose dissolved in sufficient water to make a litre will give a solution isotonic with blood plasma.

(*b*) For ionizing substances, the factor for calculating isotonic strength is M/N × 0·029, where M is the

molecular weight, and N the number of ions into which the solution dissociates.

Thus to prepare 100 ml. of a solution of potassium nitrate isotonic with blood serum—

Molecular weight of potassium nitrate = 101
Number of ions into which it dissociates = 2

Therefore percentage strength for isotonicity

$$= \frac{M}{N} \times 0{\cdot}029$$

$$= \frac{101}{2} \times 0{\cdot}029$$

$$= 1{\cdot}46 \text{ per cent.}$$

Therefore 1·46 gm. of potassium nitrate is dissolved in sufficient water to make 100 ml. and will give a solution isotonic with blood serum.

There are other methods of calculating isotonic strength, but the above is simple and yields results of sufficient accuracy. For further information see the British Pharmaceutical Codex, particularly as regards the *adjusting* of a solution to isotonic strength.

The physician may ask for a hypertonic injection. There are three reasons why hypertonic solutions can be injected.

1. If injected slowly and with skill, no harmful results may ensue and a smaller amount of solution is injected compared with an isotonic solution.
2. Hypertonic solutions are used in the treatment of varicose veins as sclerosing solutions. Thus—
   Quinine and Urethane Solution—13·33 per cent. Quinine Hydrochloride, 6·67 per cent. Urethane.
   Sodium morrhuate—5 to 10 per cent. solutions.
   Strong saline.
   Strong glucose.
   Sodium salicylate 20 to 40 per cent.
3. Hypertonic solutions may be injected intrathecally in the treatment of meningitis.

Methods of Injection.

1. *Scarification.*—The skin is scratched and a solution applied (vaccine lymph).

2. *Intradermal.*—Between the layers of the skin (Schick test toxin). The solution should be sterile.

3. *Subcutaneous* (hypodermic).—These are injections just below the skin and are generally solutions of potent medicaments (strychnine hydrochloride, morphine hydrochloride, adrenaline hydrochloride, etc.). The volume of the injection should not exceed 17 min. (1 mil). The solution should be sterile.

4. *Intramuscular injections*.—These are injections into the muscles of the arm or buttock. The response to the medicament is usually not rapid and they are used to establish a reservoir of the drug in the muscle from which gradual adsorption takes place. The injection may be (*a*) a suspension, either in water (Inj. Bismuth. B.P.) or in oil (Injection of Calomel, Injection of Mercury and Injection of Bismuth Salicylate; (*b*) a solution, either in water (Liver Extract, the organic arsenicals) or in oil (Injection of Camphor in Oil). The solutions should be sterile and isotonic. In many of the pharmacopœial injections creosote is included, not primarily as an antiseptic but as an analgesic to deaden the pain of the injection.

5. *Intravenous Injection*.—This is a very important type of injection, and the Pharmacopœia directs that all intravenous injections must be made with freshly distilled water. They may consist of a solution of a potent medicament such as strophanthin, adrenalin, insulin, etc., with a small quantity for a dose, or large quantities of isotonic solutions such as Normal Saline B.P., or Injection of Sodium Chloride and Acacia B.P., which are given to temporarily replace blood lost during hæmorrhage. The essential requirements of this type are that they must be (*a*) sterile, (*b*) prepared with freshly distilled water, (*c*) isotonic with blood plasma, (*d*) free from solid particles, (*e*) contain nothing which will cause clotting of the blood corpuscles.

A special type of intravenous injection (often known as sclerosing solutions) is used in the treatment of varicose veins, such as solutions of quinine urethane, sodium salicylate, etc. They only differ from ordinary intravenous injections in that they are not isotonic, but hypertonic. The importance of sterility cannot be too strongly stressed in intravenous injections.

6. *Intrathecal or Intraspinal Injections*.—These may consist of sera or solutions of local anæsthetics such as procaine hydrochloride. The latter type of solution is often made

more viscous by the addition of glucose, so that the solution will not flow so readily from the seat of injection and thus tend to localize the action. It is most essential that these injections are sterile, but no question of isotonicity arises.

7. *Rectal, Urethral, and Vaginal Injections.*—These preparations are strictly not comparable with the previous injections, as the question of sterility is not important, it being sufficient to prepare them with distilled water.

Rectal Injections or Enemas (Enemata) may consist of

(*a*) Food solutions such as beef peptone. This method of feeding is adopted when stomach or other conditions preclude feeding by the mouth.
(*b*) Preparations to promote evacuation of the bowels such as soap solution, etc.
(*c*) Solutions of sedatives such as opium and chloral hydrate.

In order to make them more viscous and thus render retention in the lower bowel easier, starch or mucilage of starch is often included in the formula. If starch is ordered, it must be converted into the mucilage. This is best done by rubbing it down to a very thin paste with a little cold water and then pouring it, in a thin stream with constant stirring, into a large quantity of boiling water. Unless care is exercised, the mucilage will be lumpy. Examples of Enemata will be found in the British Pharmaceutical Codex.

Urethral and Vaginal Injections. They are given by syringe, and the latter also by means of a douche can. They may consist of solutions of antiseptics and astringents.

CHAPTER XIII

PHARMACEUTICAL PROCESSES

THE British Pharmacopœia is published under the supervision of the Medical Council, and undergoes revision at certain intervals. It must be regarded by the pharmacist and the physician as having all the authority of an Act of Parliament. The drugs, tests, and processes mentioned in it are said to be "Official." The following pages will briefly describe the chief pharmaceutical processes referred to in it.

The student will probably discover that many of these are but repetitions of processes already practised by him in the chemical laboratory—as precipitation, crystallization, etc.; others, however, will be found to be peculiar to pharmacy—as percolation, infusion, etc.; and it will be advisable for him, before entering upon the study of the various preparations, to glance at a few of these more important processes—especially to those that are common to many groups of preparations, as–

Adsorption.—This is the phenomenon of surface condensation or concentration on a surface as distinct from **absorption,** when a substance is distributed throughout the mass. Adsorption plays an important part in pharmaceutical operations. Charcoal adsorbs gases and colouring matter. Fuller's earth is used to adsorb Vitamin B, from solution (Pulvis Vitamini B_1, B.P.).

Calcination is the process of purifying a solid by strongly heating it and driving off volatile impurities. Thus mineral ores are calcined prior to smelting to drive off sulphur and arsenic. The term is also applied to the heating of calcium and magnesium carbonates with the production of oxides and the driving off of carbon dioxide.

Carbonization is the process by which organic substances, like coal, bones and wood, are heated without access of air, so that they are decomposed, leaving a residue of coke, animal and wood charcoal respectively, and volatile decomposition products are driven off and condensed. The process is also known as Destructive Distillation, and many pharmacopœial substances are prepared in this manner, such as phenol, wood tar, coal tar, ichthammol, etc.

Clarification is the purification of a galenical preparation by the removal of suspended solids, with the consequent production of a clear bright preparation. It may be effected by—

(*a*) Filtration. Ordinary filtration through filter-paper, or pressure filtration through special filter packs consisting of either a column of filter-papers (stream-line filter) or calico. Very viscous liquids, such as oils or syrups, are usually filtered through felt bags or the filtration through paper hastened by using a hot water-jacketed funnel. Ordinary filtration through paper or fabric may be hastened

by using a Buchner funnel and sucking the liquid through by reduced pressure. Coarse particles may be removed by filtering or straining through calico, flannel or muslin.

(*b*) Depuration or clarification by heat. This consists of gently heating the preparation, when the impurities either rise to the top and are skimmed off (purified honey) or coagulate and are filtered out. The latter is a common process in the preparation of extracts (Extract of Liquorice) whereby the protein matter is coagulated.

(*c*) Addition of other substances, such as talc, kieselguhr, pulped paper. If an alcoholic solution of a volatile oil be cloudy, it can be readily clarified by the addition of these substances and filtration.

(*d*) Animal charcoal. This is employed to remove colour, the liquid being shaken with a little of it and then filtered.

(*e*) Centrifugal separation. The throwing down of particles by placing the liquid in a centrifuge and revolving at a high speed. A modern centrifuge designed for continuous use is the Sharples Supercentrifuge, and is very useful for galenical clarification.

Colation is the name given to straining. (See Clarification.)

Comminution is the process of reducing substances to small particles. The degree of comminution of drugs varies according to the particular object in view. It may range from coarsely sliced or coarsely powdered (to facilitate extraction with a solvent) to a very fine powder known as an *impalpable powder*. The latter is so fine as not to be gritty to the palate, and is required with those drugs which are swallowed in the powdered state, such as liquorice, rhubarb, senna, etc. It is usually necessary to thoroughly dry a drug before attempting to reduce it to a powder. Coarse comminution may be effected by slicing with a root-cutter or bruising in a metal mortar ; fine comminution by grinding in a mortar, edge-runner mill, ball mill, coffee mill or disintegrator.

Crystallization is the process which bodies undergo is passing from the liquid or gaseous state to assume definite and regular geometrical forms called crystals. This process is generally directed to be carried out by the cooling or evaporation of a solution containing the substance to be crystallized, or more rarely it is ordered to be effected by

fusion, as in the case of some of the metals; by sublimation, as benzoic acid and corrosive sublimate; or by precipitation, as in the instance of the red iodide of mercury. In obtaining crystals by evaporation the liquid is either boiled till its volume is reduced by the loss of vapour, or it may be kept at a lower temperature than the boiling-point for a longer time till the same effect is produced, and when the concentration has proceeded so far that a scum or pellicle forms on its surface, the liquid is set aside to cool, and as the temperature falls crystals form. When they have ceased to grow or increase, the fluid part, which is now called the "mother liquor," is poured off, and the crystals drained and dried. A second or third crop may be obtained from the mother liquor by further evaporation and cooling, as in the first instance. The process is hastened by the presence of foreign bodies, as threads or sticks, round which the crystals quickly gather; or by agitation, in which case the crystals will be found to be small. The slower the process the larger and more regular will be the crystals.

Decoction is the process of boiling a coarsely comminuted drug with water for a definite time and then straining. Decoctions resemble infusions except that the drugs do not contain volatile constituents. Decoctions, unless they contain a preservative, will not keep.

Distillation consists of the conversion of a volatile liquid into a vapour by means of heat, and the condensation of the vapour back again into the liquid state. The apparatus consists of a retort or distilling flask, a condenser and a receiver.

Distillation may be used for (*a*) the purification of a volatile liquid from non-volatile impurities; (*b*) the separation of a mixture of liquids which have different boiling-points (Fractional Distillation); (*c*) the blending of volatile substances such as volatile oil and water, as in the preparation of the Distilled Aromatic Waters; (*d*) the dry heating, with decomposition of solid substances and the condensation of the volatile decomposition products (Destructive Distillation).

The condenser consists of a glass or metal tube or spiral, which may be air-cooled or water-cooled. A reflux condenser is one which is so arranged that the condensed liquid runs back into the distilling flask, and is used in operations when

a drug has to be boiled for a long period with a volatile solvent.

Drying or Desiccation.—Vegetable drugs are dried in order to (*a*) reduce the bulk, (*b*) prevent the growth of moulds during storage, (*c*) facilitate comminution. The temperature and conditions of drying vary very much according to the drug. Drugs like digitalis, strophanthus, squill, etc., whose active principles readily hydrolyse and become inactivated, require to be rapidly dried at as low a temperature as possible. This is generally done at about 40° C. in a good current of air. On the other hand, drugs like gentian, vanilla, cacao seeds, valerian, etc., require slow drying in order that certain changes, which improve either the appearance, taste or odour, may take place.

Elutriation is fractional sedimentation, and consists of powdering a substance which is insoluble in water, shaking it with water, allowing to stand for a certain time during which the heavy gritty particles will settle to the bottom, and drawing off the supernatant liquid. This is then allowed to stand, when the fine particles settle out and are collected and dried. Native chalk and china clay are so treated with the production of prepared chalk (Creta B.P.) and kaolin respectively.

Expression is the process by which a menstruum is squeezed out from a marc or the juice or oil from a drug. It is performed in a press which may be worked by hand or by hydraulic power.

Evaporation is the conversion of the surface layer of a liquid into a vapour and takes place at all temperatures. It is a surface action only, and should be distinguished from boiling, during which vapour is formed in any part of the liquid at its boiling-point. The rate of evaporation is governed by: (*a*) The surface area. The greater the area the greater the rate of evaporation. Thus evaporating pans are wide and shallow; (*b*) the temperature and pressure. The rate increases with rising temperature and with diminishing pressure. This is taken advantage of in evaporation under reduced pressure (or *in vacuo*), whereby evaporation (or distillation) can be greatly increased without raising the temperature unduly. Certain preparations in the Pharmacopœia are required to be prepared under reduced pressure to minimise decomposition, such as Liquid Extract of Ergot, Liquid Extract of Hyoscyamus, etc.

Infusion is the process of extracting a drug by adding boiling or cold water, allowing to stand for a definite time (usually 15 minutes), and straining off. The process is suitable for drugs containing water-soluble and volatile constituents. If the drug contains starch (such as calumba) cold water must be used. They are designed to be readily made preparations, and filtration is avoided by having the drug in a coarsely comminuted condition so that the exhausted residue can be removed by straining.

Infusions, unless they contain alcohol, will not keep, and the Pharmacopœia requires that fresh infusions shall be used within 12 hours of their preparation.

Isotonic Solutions are solutions which exert the same osmotic pressure. In Pharmacy two standards are used, Blood Plasma for intravenous injections, and Lacrymal Secretion for eye drops or solutions. Blood Plasma is isotonic with 0·9 per cent. sodium chloride solution, and Lacrymal Secretion with 1·4 per cent. sodium chloride solution. Solutions exerting an osmotic pressure higher than the standard are said to be hypertonic, and those with a lower one, hypotonic.

Levigation is the process of reducing a substance to a very fine powder by rubbing down with some liquid in which it is soluble. The process is a very important one in the preparation of ointments, particularly eye ointments containing yellow mercuric oxide, also in the preparation of Oleated Mercury B.P., in which the success of the process depends upon the good levigation of the yellow mercuric oxide with the small quantity of liquid paraffin.

Lixiviation is the process of mixing a substance with a solvent and extracting a soluble constituent by pouring off from the insoluble residue, as is done in the extraction of black ash in the preparation of sodium carbonate.

Maceration is a process of extracting a drug with a solvent by placing the two in contact, allowing to stand for seven days, shaking occasionally, straining, pressing the marc and mixing the expressed liquid with the strained liquid, clarifying by subsidence or filtration. It is an official process for the making of several tinctures, and is suitable for gummy or resinous drugs which cannot be percolated.

Percolation is a process for extracting a drug by packing it in a cylindrical or conical vessel, known as a percolator, and passing the solvent slowly through. The solution of the active principles passes on into the receiver, thus causing fresh solvent to be brought into contact with the drug. The official process is described as follows: "Moisten the solid materials with a sufficient quantity of menstruum, set aside for four hours in a well-closed vessel, pack in a percolator, and add sufficient of the menstruum to saturate the materials. When the liquid commences to drop from the percolator close the outlet, add sufficient of the menstruum to leave a layer above the drug, and allow it to macerate for 24 hours. Allow percolation to proceed slowly, until the percolate measures about three-fourths of the volume required for the finished tincture. Press the marc, mix the expressed liquid with the percolate, and add sufficient of the menstruum to produce the required volume. Clarify by subsidence or by filtration."

Percolation is a better extraction process than maceration, and if it can be employed, it is employed. It is particularly suitable for fibrous drugs, such as roots, barks, fruits, seeds, leaves, etc. It is not suitable for drugs containing much mucilage or resin, as these tend to clog in the percolator. The drug must be in a convenient size powder, not too fine to clog the percolator, nor too coarse to prevent the menstruum to run through too quickly. The percolator is packed, first with a short layer of tow and sand, and then with the drug. The latter must be carefully packed so as not to leave channels, nor too tightly to unduly restrict the flow. Fig. 23 shows some typical percolators.

Powders.—The Pharmacopœia standardizes the size of a powdered drug by specifying the sieves through which it will and will not pass. Thus:

Coarse powder (10/44) is a powder of which all the particles will pass through a No. 10 sieve and not more than 40 per cent. through a No. 44 sieve.

Moderately coarse powder (22/60) passes a No. 22 sieve, but not more than 40 per cent. passes a No. 60 sieve.

Other powders are:

Moderately fine powder (44/85).

Fine powder (85) which entirely passes a No. 85 sieve.

Very fine powder entirely passes a specified silk sieve.

The number specifying a sieve indicates the number of meshes included in a linear inch parallel to the strands of standard gauge wires. Thus a No. 22 sieve has 22 meshes to the linear inch.

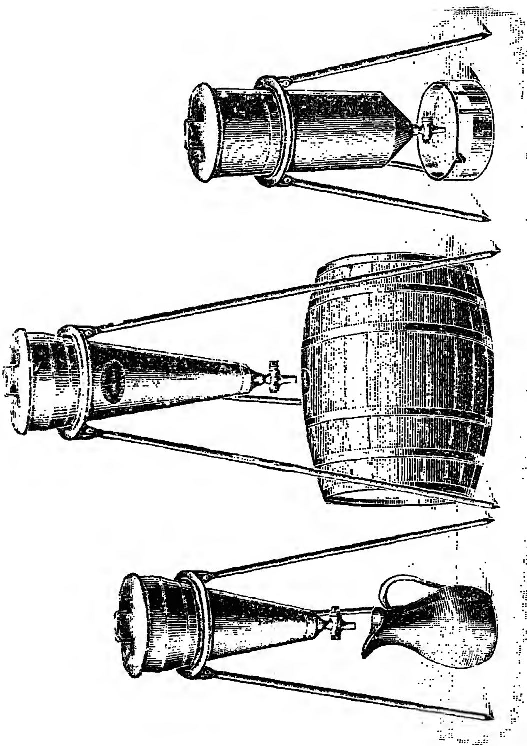


FIG. 23.—Some typical percolators.

Precipitation is the process of forming an insoluble substance from a solution by chemical or physical means. Thus if a solution of potassium iodide be added to a solution of

mercuric chloride, a red precipitate of mercuric iodide is formed. An alteration in the solvent may sometimes cause precipitation, thus when Spirit of Camphor is added to water Camphor is thrown out of solution. Heat will sometimes bring it about, for in the preparation of Extract of Liquorice, protein matter is precipitated by raising the extractive to boiling. In the dispensing of certain mixtures it may happen that a precipitate is unavoidable owing to reaction between the medicaments. It may, however, be possible, by manipulation, to cause the particles to be very fine instead of coarse, thus facilitating suspension.

Solution.—A saturated solution is one which contains the maximum amount of substance (solute) in solution at the particular temperature. The solubility of a solute usually increases with rise of temperature, and the Pharmacopœia states solubilities at 15·5° unless otherwise specified.

A supersaturated solution is one in a metastable (or unstable) condition containing an amount of solute in excess of that required for saturation. On shaking or on the addition of a solid particle the solution readily deposits its excess of solute and returns to the saturated condition.

Standardization as applied to galenical preparations denotes the fixing of a definite active principle content, those made from alkaloids being estimated chemically and adjusted to a specified alkaloidal content. The strength of less potent galenicals is based upon the relation between the weight of drug taken and the volume of galenical produced. Certain very potent drugs such as digitalis, strophanthus, insulin, etc., which cannot be estimated chemically, have to be tested by a biological method on animals, and adjusted to a specified standard.

Sublimation is the conversion of a solid into a vapour and the reconversion into the solid state without passing through a liquid phase. Thus camphor when heated readily vaporizes and the vapour will readily condense to the solid state again, but there is no intermediate liquid state. Sublimation is used to purify volatile solid from non-volatile impurities, the latter being left behind. The following are purified in this way:—arsenic, benzoic acid, camphor, calomel, mercuric chloride, salicylic acid.

CHAPTER XIV

WEIGHTS AND MEASURES OF THE BRITISH PHARMACOPŒIA

WITH THE LEGAL CONTRACTIONS AUTHORISED UNDER THE WEIGHTS AND MEASURES ACT

METRIC SYSTEM

Measures of Mass (Weights)

1 Milligram (Mg.) = the 1000th part of 1 gramme or 0·001 gm.
1 Gramme (gm.) = the 1000th part of 1 Kilogram.
1 Kilogram (kg. or kilog.) is the standard or International Kilogramme.

For the purpose of writing prescriptions, in order to avoid the possibility of confusion between "gramme" and "grain," the symbol "G" should be used as the contraction for "gramme."

Measures of Capacity (Volumes)

1 Millilitre or Mil (Mil) = the 1000th part of 1 litre.
1 Litre (Lit.) = 1 kilogram of water.
1 Litre measures about 1000·028 cubic centimetres.

Measures of Length

1 Micron (μ) = the 1000th part of 1 millimetre or 0·001 mm.
1 Millimetre (mm.) = the 1000th part of 1 metre or 0·001 m.
1 Centimetre (cm.) = the 100th part of 1 metre or 0·01 m.
1 Metre (m.) = 1·0 m.

IMPERIAL SYSTEM

Measures of Mass (Weights)

1 Grain (gr.) = the 7000th part of 1 pound.
1 Ounce (Avoir.) (oz.) = 437·5 grains.
1 Pound (Avoir.) (lb.) = 7000·0 grains, and is the standard pound as defined in the Weights and Measures Act, 1878.

Measures of Capacity (Volumes)

1 Minim (min.) = the 60th part of 1 fluid drachm.
1 Fluid Drachm (fl. dr.) = 60 min.
1 Fluid Ounce (fl. oz.) = 8 fl. dr.
1 Pint (pt.) = 20 fl. oz. is the Imperial Standard Pint as defined in the Weights and Measures Act, 1878.

RELATION OF CAPACITY TO MASS (IMPERIAL)

1 Minim	= the vol. at 16·7° (62° F.) of 0·9114583 gr. of water.
1 Fluid Drachm	= the vol. at 16·7° (62° F.) of 54·6875 gr. of water.
1 Fluid Ounce	= the vol. at 16·7° (62° F.) of 1 oz. or 437·5 gr. of water.
109·7143 Minims*	= the vol. at 16·7° (62° F.) of 100 gr. of water.

RELATIONS OF METRIC AND IMPERIAL MEASURES

Mass

1 Milligram (mg.)	=	0·015 grain nearly.
1 Gramme (gm.)	=	15·4323564 grains.
1 Kilogram (Kg.)	=	15432·3564 grains, or 35·274 ounces nearly, or 2·2046 pounds nearly.
1 Grain (gr.)	=	0·0648 gramme nearly.
1 Ounce (Avoir.) (oz.)	=	28·350 grammes nearly.
1 Pound (Avoir.) (lb.)	=	453·59 grammes nearly.

Capacity

1 Millilitre or Mil (Mil)	=	16·9 minims nearly.
1 Litre (Lit.)	=	1·75980 pints, or 35·196 fluid ounces nearly.
1 Minim (min.)	=	0·0592 mil nearly.
1 Fluid Drachm (fl. dr.)	=	3·5515 mils nearly.
1 Fluid Ounce (fl. oz.)	=	28·4123 mils nearly.
1 Pint (pt.)	=	568·2454 mils nearly, or 0·5682 litre nearly.

Length

1 Micron (μ)	=	0·00003937 inch.
1 Millimetre (mm.)	=	0·039370 inch.
1 Centimetre (cm.)	=	0·39370 inch.
1 Metre (m.)	=	39·370113 inches.
1 Inch (in.)	=	25·3999 millimetres.

The above weights and measures of the Metric and Imperial Systems are the ones used in stating the quantities and standards in the Pharmacopœia, but in the prescribing of medicines the Apothecaries' System is still generally used and the student must appreciate the relationship. The following are the symbols and signs used in prescriptions :

Gr.i. = granum, 1 grain $= \frac{1}{7000}$ part of 1 pound.
†℈i. = scrupulum, 1 scruple = 20 grains.

* Taken as 110 minims throughout the Pharmacopœia.
† It is not customary to use the sign of the scruple ℈ after liquids.

ʒi.	= drachma, 1 drachm	= if a solid, 60 grains; if a liquid, 60 minims.
℥i.	= uncia, 1 ounce	= if a solid, 8 drachms or 480 grains; if a liquid, 8 fluid drachms or 480 minims.
♏i.	= minimum, 1 minim	= $\frac{1}{60}$ part of a fluid drachm.
Oi.	= octarius, 1 pint	= ℥xx. or 1 imperial pint.
Ci.	= congius, 1 gallon	= 8 pints.

The student should note very carefully that:

℥i. following a solid	= 480 grains.
℥i ,, liquid	= 480 minims (= 1 fl. oz. imperial).

Also that ℥i. of *water* = 480 minims and weighs 437·5 grains; and also from this, that 110 minims of water weighs 100 grains (approx.).

1 oz. = 1 imperial ounce and = 437·5 grains.
1 oz. of *water* (i.e., 437·5 grains) measures ℥i. or 480 minims.
Oi. of *water* = 20 ozs. = 20 × 437·5 grains = 20 × 480 minims.
Ci. of *water* = 10 lb. = 70,000 grains.

DOMESTIC MEASURES

The following should be regarded as the official equivalents of the domestic measures, but when possible all mixtures prescribed by the physician should be measured in properly graduated medicine glasses. This is particularly important when an unusually large dose of a potent ingredient is prescribed. In this case the dispenser should always label the mixture "One *measured* tablespoonful," etc.

A tea-spoonful	Cochleare minimum or Cochleare parvum	= 1 fluid drachm (ʒj.)
A dessert-spoonful	Cochleare medium	= 2 fluid drs. (ʒij.)
A table-spoonful	Cochleare amplum or Cochleare magnum	= 4 fluid drs. or ½ oz. (ʒiv. or ℥ss.)
A wine-glassful	Cyathus vinarius	= 2½ fluid oz. (℥iiss.)

The wine-glass (i.e. the sherry-glass) is generally stated to contain 1½ to 2 ounces. It will, however, be nearly always found to contain at least 2½ ounces, or the eighth part of an imperial pint. The writer believes that most physicians, when ordering medicine to be taken in doses of a wine-glassful, calculate upon the wine-glass containing at most 2

ounces. This idea arises from the old wine-glassful being equal to the $\frac{1}{8}$ part of the old wine pint of 16 ounces.

A small teacup contains on an average about 7 fluid ounces, and a breakfast-cup about 12 fluid ounces. These figures are much above those mentioned in most books.

The common glass tumbler holds $\frac{1}{2}$ pint, and is a fairly accurate measure.

The mistake of counting drops as minims has been already referred to on p. 159.

PERCENTAGE SOLUTIONS

It often happens that percentage solutions are ordered on prescriptions, and in this connection the Pharmacopœia uses the following symbols:

Per cent. w/w expresses the number of grammes of solute in 100 grammes of solution.

Per cent. w/v expresses the number of grammes of solute in 100 mils of solution.

Per cent. v/v expresses the number of mils of solute in 100 mils of solution.

If, however, on a prescription none of the symbols w/w, w/v, or v/v are used, it should be interpreted as follows:

If a solid in a liquid, then w/v (weight in volume).
If a liquid in a liquid, then v/v (volume in volume).
If a solid in a solid, then w/w (weight in weight).

Thus a 10 per cent. or 1 in 10 solution is prepared by dissolving 10 grammes of a solid or 10 mils of a liquid in sufficient solvent to produce 100 mils.

In the Apothecaries' System, a 10 per cent. solution would be prepared by dissolving 10 grains of a solid in sufficient solvent to produce 110 minims of solution, or 10 minims of a liquid made up to 100 minims with the solvent.

℥i. of a 10 per cent. solution, solid in liquid = 44 grains (approximately) in ℥i. of solution.

℥i. of a 10 per cent. solution, liquid in liquid = 48 minims in ℥i. of solution.

RELATION OF ENGLISH TO METRIC MEASURES

1	Minim	=	·059	millilitre
2	Minims	=	·118	,,
3	,,	=	·178	,,
4	,,	=	·237	,,

RELATION OF ENGLISH TO METRIC MEASURES—*continued*

5 Minims	=	·296	millilitre
6 ,,	=	·355	,,
7 ,,	=	·414	,,
8 ,,	=	·473	,,
9 ,,	=	·533	,,
10 ,,	=	·592	,,
11 ,,	=	·651	,,
12 ,,	=	·710	,,
13 ,,	=	·769	,,
14 ,,	=	·828	,,
15 ,,	=	·888	,,
16 ,,	=	·947	,,
17 ,,	=	1·007	,,
18 ,,	=	1·066	,,
19 ,,	=	1·125	,,
20 ,,	=	1·184	,,
25 ,,	=	1·480	,,
30 ,,	=	1·776	,,
35 ,,	=	2·072	,,
40 ,,	=	2·368	,,
45 ,,	=	2·664	,,
50 ,,	=	2·960	,,
55 ,,	=	3·256	,,
1 Fluid Drachm	=	3·5515	,,
2 Fluid Drachms	=	7·103	,,
3 ,, ,,	=	10·654	,,
4 ,, ,,	=	14·206	,,
5 ,, ,,	=	17·757	,,
6 ,, ,,	=	21·309	,,
7 ,, ,,	=	24·860	,,
1 Fluid Ounce	=	28·412	,,
2 Fluid Ounces	=	56·824	,,
3 ,, ,,	=	85·236	,,
4 ,, ,,	=	113·649	,,
5 ,, ,,	=	142·061	,,
10 ,, ,,	=	284·122	,,
15 ,, ,,	=	426·183	,,
20 ,, ,,(1 pt.)	=	568·245	,,
40 ,, ,,(1 qt.)	=	1136·49	,,

RELATION OF ENGLISH TO METRIC WEIGHTS

1 Grain	=	·0648	gm.
2 Grains	=	·1296	,,
3 ,,	=	·1944	,,
4 ,,	=	·2592	,,
5 ,,	=	·3240	,,
6 ,,	=	·3888	,,
7 ,,	=	·4536	,,
8 ,,	=	·5184	,,
9 ,,	=	·5832	,,

RELATION OF ENGLISH TO METRIC WEIGHTS—*continued*

10 Grains	=	·6480	gm.
11 ,,	=	·7128	,,
12 ,,	=	·7776	,,
13 ,,	=	·8424	,,
14 ,,	=	·9072	,,
15 ,,	=	·9720	,,
15·432 ,,	=	1 Gramme	
1 Scruple (20 grains)	=	1·2959	gm.
2 Scruples (40 grains)	=	2·5919	,,
3 ,, or 1 Drachm	=	3·8879	,,
1 Ounce (Troy)	=	31·1034	,,

¼ oz.	(Avoir.)	or	109·375	gr.	=	7·087375	gms.
½ ,,	,,	or	218·75	,,	=	14·17476	,,
1 ,,	,,	or	437·5	,,	=	28·34953	,,
2 ,,	,,	or	875	,,	=	56·699	,,
3 ,,	,,	or	1312·5	,,	=	85·0486	,,
4 ,,	,,	or	1750	,,	=	113·3981	,,
5 ,,	,,	or	2187·5	,,	=	141·7477	,,
6 ,,	,,	or	2625	,,	=	170·097	,,
7 ,,	,,	or	3062·5	,,	=	198·4466	,,
8 ,,	,,	or	3500	,,	=	226·7962	,,
9 ,,	,,	or	3937·5	,,	=	255·1458	,,
10 ,,	,,	or	4375	,,	=	283·495	,,
11 ,,	,,	or	4812·5	,,	=	311·8449	,,
12 ,,	,,	or	5250	,,	=	340·1943	,,
13 ,,	,,	or	5687·5	,,	=	368·5439	,,
14 ,,	,,	or	6125	,,	=	396·8933	,,
15 ,,	,,	or	6562·5	,,	=	425·243	,,
16 ,,	,, (1 lb.)	or	7000	,,	=	453·59243	,,

RELATION OF METRIC TO ENGLISH WEIGHTS

1 Milligram, or ·001 gramme	=	nearly				$\frac{1}{64}$	grain.
1 Gramme	=	,,				15½	grains.
5 Grammes	=	,,				77⅙	,,
10 ,,	=	,,				154⅓	,,
20 ,,	=	,,				308⅔	,,
30 ,,	=	,,	1	ounce	and	25½	,,
40 ,,	=	,,	1	,,	and	179¾	,,
50 ,,	=	,,	1	,,	and	334	,,
60 ,,	=	,,	2	ounces	and	51	,,
70 ,,	=	,,	2	,,	and	205¼	,,
80 ,,	=	,,	2	,,	and	359½	,,
90 ,,	=	,,	3	,,	and	76⅓	,,
100 ,,	=	,,	3	,,	and	230¼	,,
200 ,,	=	,,	7	,,	and	24	,,
300 ,,	=	,,	10	,,	and	254¾	,,
400 ,,	=	,,	14	,,	and	48	,,
500 ,,	=	,,	17	,,	and	278½	,,
600 ,,	=	,,	21	,,	and	71¾	,,

RELATION OF METRIC TO ENGLISH WEIGHTS—*continued*

700 Grammes		=nearly	24 ounces	and 302$\frac{1}{2}$ grains.
800 ,,		= ,,	28 ,,	and 96 ,,
900 ,,		= ,,	31 ,,	and 326$\frac{1}{3}$,,
1000 ,,	(1 kilogram)	= ,,	35 ,,	and 120 ,,

RELATION OF METRIC TO ENGLISH MEASURES

1 millilitre		= nearly				16·95 minims.
2 millilitres		= ,,				33·9 ,,
3 ,,		= ,,				50·8 ,,
4 ,,		= ,,			1 dr.	7·61 ,,
5 ,,		= ,,			1 dr.	24·5 ,,
6 ,,		= ,,			1 dr.	41·41 ,,
7 ,,		= ,,			1 dr.	58·32 ,,
8 ,,		= ,,			2 drs.	15·22 ,,
9 ,,		= ,,			2 drs.	32·5 ,,
10 ,,		= ,,			2 drs.	48·9 ,,
15 ,,		= ,,			4 drs.	13·4 ,,
20 ,,		= ,,			5 drs.	37·8 ,,
25 ,,		= ,,			7 drs.	2·4 ,,
30 ,,		= ,,	1 oz.		0 drs.	26·8 ,,
40 ,,		= ,,	1 oz.		3 drs.	15·7 ,,
50 ,,		= ,,	1 oz.		6 drs.	4·7 ,,
75 ,,		= ,,	2 oz.		5 drs.	7·1 ,,
100 ,,		= ,,	3 oz.		4 drs.	9·4 ,,
500 ,,		= ,,	17 oz.		4 drs.	47 ,,
000 ,,	(1 litre)	= ,,	35 oz.		1 dr.	34 ,,

CHAPTER XV

PRESCRIPTION WRITING

The Model Prescription should consist of the following parts :

1. The Superscription.
2. The Inscription.
3. The Subscription.
4. The Signature.

1. The *Superscription*, which consists of the letter ℞., originally was used, it is supposed, to represent the symbol of the planet Jupiter, at a time when much of the virtue of

a combination appeared to rest upon the deity or presiding star. By common consent, it is now regarded as representing the imperative mood of the Latin verb Recipio, to take; hence the origin of the ordinary term "recipe." The French physicians commence their prescriptions with P., or Prenez.

2. The *Inscription* may be called the *body* of the prescription; it includes the names of the substances to be administered, with their quantities, written in Latin, and as it is the most important part of the prescription, it will be referred to presently at more length.

3. The *Subscription* is made up of the directions (in Latin) for the guidance of the dispenser; thus *misce*, often written *m.*, is frequently the only part in a prescription which belongs to the subscription.

4. The *Signature* includes the directions or instructions intended for the benefit of the patient. It is frequently written by the prescriber in English, and many recommend that Latin should never be used for this part of the prescription.

Mistakes are certainly liable to occur if the signature be written carelessly, or if incorrect Latin be employed, but the same reasons which have determined the use of this language for prescriptions from an early time, apply equally well to the signature. Thus a prescription written in Latin can be read and understood by a pharmaceutical chemist or physician in every civilised country. Abbreviations and contractions can be employed without fear of being misunderstood, which could not be the case if any other language were substituted; we are thus often able, by a single letter, to express the meaning of several English words.

It is often absolutely *necessary* to write the prescription in such a way that the patient may remain ignorant of the nature of its contents.

The use of long and elaborate Latin phraseology is to be condemned in prescribing, and the student, when he feels any difficulty in expressing himself in this tongue, had certainly better fall back upon his English when writing the signature. This he can do by using the Latin word Signa, after which the signature may be written in *unabbreviated* English.

The patient's name is written at the top or bottom of the recipe, preferably the top, as it is thus less liable to be overlooked or mistaken than if written where space is often

limited. The prescriber's initials generally follow at the corner of the document opposite to the physician's right hand, and the date is written on the opposite corner.

It is hardly necessary to remind the student of the necessity of writing *clearly* and *legibly*, and of avoiding the use of such contractions as might lead to mistakes.

The *body* or inscription of a model prescription should contain the following:

The *Basis*, or principal active ingredient (*basis*).
The *Adjuvant*, or *Auxiliary*, to assist its action (*adjuvans*).
The *Corrective*, to correct or diminish some undesirable quality (*corrigens*).
The *Vehicle*, or *Excipient*, to give a suitable form for administration (*vehiculum*).

The following prescription may be regarded as a type of a very commonly ordered combination of remedies :

℞.	. . . .	SUPERSCRIPTION.
(Basis.)	*Pot. Acet.* ʒv.	INSCRIPTION.
(Adjuvant.)	*Tinct. Digitalis.* ʒj.	
(Corrective.)	*Syr. Aurantii* ℥j.	
(Vehicle.)	*Inf. Scopar. ad* ℥viij.	
Misce, fiat mist.	. . . . .	SUBSCRIPTION.
Cpt. Cochl. mag. ii. 4ta. q.q. hora ex paul. aquæ.	. . . . . .	SIGNATURE.

Without abbreviations or contractions it would read thus :—

Recipe

Potassii Acetatis *drachmas quinque.*
Tincturæ Digitalis *drachmam unam.*
Syrupi Aurantii *unciam unam.*
Infusum Scoparii ad *uncias octo.*

Misce, fiat mistura. Capiat cochlearia duo magna quartâ quâque horâ ex paululo aquæ.

NOTE.—The student should not confound the *initials* of the prescriber with that portion of the prescription called the signature—i.e., the directions to the patient.

The student will find benefit from a careful study of the following pages, in which the Latin of the above prescription is arranged according to the English idiom, and each word parsed and translated.

Latin Idiom.

Recipe Potassii Acetatis drachmas quinque.

℞. (Recipe) ..	v. irr. tr. im. m. 2nd per. s., to agree with its nom. *Tu*—"thou" (understood). Rule i., recipi-o, recep-i, receptum, recipere.	Take thou
v (quinque) ..	num. adj. indec. ac. pl. qual. and agreeing with drachmas. Rule ii.	five
ʒ (drachmas) ..	n. f. ac. pl. Rule viii. (*a*), drachma—æ.	drachms
Acet. (acetatis) ..	n. f. gen. s. qual. drachmas. Rule vi. (*a*), acetas—atis.	of acetate
Pt. (potassii) ..	n. n. gen. s. qual. acetatis. Rule vi. (*a*), potassium—ii.	of potassium.

Latin Idiom

Recipe Digitalis Tincturæ drachmam unam.

℞. (Recipe) ..	(understood)	Take thou
(unam) ..	num. adj. ac. s. qual. and agreeing with drachmam. Rule *ii.*, unus—a—um.	one
ʒ (drachmam) ..	n. f. ac. s. gov. by recipe. Rule viii. (*a*), drachma—æ.	drachm
Tinct. (tincturæ)	n. f. gen. s. qual. drachmam. Rule vi. (*a*), tinctura—æ.	of the tincture.
Digit. (digitalis)	n. f. gen. s. qual. tincturæ. Rule vi. (*a*), digitalis—is.	of digitalis.

Latin Idiom

Recipe Aurantii Syrupi unciam unam.

℞. (Recipe) ..	(understood)	Take thou
j (unam) ..	(parsed as before)	one
℥ (unciam) ..	n. f. ac. s. gov. by recipe. Rule viii. (*a*), uncia—æ.	ounce
Syr. (syrupi) ..	n. m. gen. s. qual. unciam. Rule vi. (*a*), syrupus—i.	of syrup
Aur. (aurantii) ..	n. neu. gen. s. qual. syrupi. Rule vi. (*a*), aurantium—ii.	of orange.

Latin Idiom

Recipe Infusum Scoparii ad uncias octo.

℞. (Recipe) ..	(understood)	Take thou
*Infus.** (Infusum)	n. neu s. acc. gov. by recipe. Rule viii. (*a*), infusum—i.	infusion

NOTE.—*Some authorities put Infusum in the genitive (infusi)—a partitive genitive—i.e. "of infusion." In the same way, where the

Scop. (scoparii) ..	n. masc. gen. s. qual. infusum. Rule vi. (*a*), scoparius—ii.	of broom
Ad	prep. gov. uncias. Rule viii. (*b*)	up to
viij (octo) ..	num. adj. indec. qual. uncias. Rule ii	eight
℥ (uncias) ..	n. f. ac. pl. gov. by ad. Rule viii. (*b*), uncia—æ.	ounces.

NOTE.—The student must have a clear idea of the meaning of this "Ad." It means that the dispenser, after measuring the other ingredients, must add enough of the infusion to make the entire quantity measure 8 oz.

Latin Idiom

Misce, fiat mistura.

M. (misce) ..	v. trans. imp. m. p. t. agreeing with and gov. by tu (understood). Rule i., misceo, -ui, mixtum or mistum, miscere.	Mix thou, or mix
Mist. (mistura) ..	n. f. nom. s. governing fiat. Rule i., mistura—æ.	let a mixture
Ft. (fiat) ..	v. used as passive of facio, pres. sub. 3rd s., used as imp. gov. by and agreeing with mistura; fio, factus sum, fieri; to be made or become.	be made.

Latin Idiom

Capiat cochlearia magna duo quartâ quâque horâ ex aquæ paululo.

Cpt. (capiat) ..	irr. v. tr. sub. m. pr. t. 3rd per. s. agreeing with and gov. by is (understood). Rule i., capio, cepi, captum, capere, the present subjunctive used as an imperative. Rule x. (*a*).	He may take, or let him take
ij (duo)	num. adj. ac. pl. neut. qual. and agreeing with cochlearia. Rule ii., duo—æ—o.	two
Mag. (magna) ..	adj. ac. pl. neut. qual. and agreeing with cochlearia. Rule ii., magnus—a—um.	large
Coch. (cochlearia)	n. ac. pl. neut. gov. by capiat. Rule viii. (*a*) cochlear—is.	spoonfuls

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student meets *Aquam ad* ℥—, in the different prescriptions throughout the Fourth Part of this work, he may substitute *Aquæ ad* ℥. Either form is correct.

q.q. (quâque)	..	pron. indef. abl. s. qualifying and agreeing with hora. Rule ii., quisque, quæque, quodque.	at each
4tâ (quartâ)	..	num. adj. abl. s. qualifying and agreeing with hora. Rule ii., quartus—a—um.	fourth
Horâ ..	..	n. f. abl. s. Rule ix. (*a*), hora —æ.	hour
Ex ..	..	prep. Rule ix. (*c*).	out of (in)
Paul. (paululo)	..	adj. abl. s. used as a noun, gov. by ex; paululus—a—um.	a little
Aq. (aquæ)	..	n. f. gen. s. qual. paululo. Rule vi., aqua—æ.	of water.

GRAMMATICAL AIDS TO PRESCRIPTION WRITING

Two languages differ in *words*, *inflections*, and *idioms*.

"A student who wishes to read the Latin language must thus understand the *meaning* of its words, the *force* of its inflections, and the *nature* of its idioms."

As far as the *words* are concerned, a limited knowledge of this language, and one sufficient for the intelligent reading and writing of physicians' prescriptions, may be obtained from the following brief vocabulary.

The *inflections* may be learned from any Latin grammar; whilst the student may obtain a fair conception of the *idioms* or order of words from a careful study of the few important rules of Syntax which follow.

A FEW RULES OF LATIN SYNTAX, APPLICABLE TO THE CONSTRUCTION OF PHYSICIANS' PRESCRIPTIONS.

Syntax is generally divided into two parts—CONCORD and GOVERNMENT.

Concord is the agreement between two Latin words, one influencing the other. There are three concords:

1. A verb, with its subject (as Rule I).
2. Adjectives, with the nouns which they qualify. (Rule II.)
3. The Relative, with its antecedent. (Rule III.)

RULE I

A personal verb agrees with its subject or nominative, in number and person; as, *Ego tero*—I rub; *Tu sumas*—You may take; *Id fiat*—It may be done.

In prescription writing, the *active* voice of verbs is gener-

ally only used in the 2nd person singular of the imperative mood, and 3rd person singular or plural of the present subjunctive.

The use of the *passive* voice is generally confined to the 3rd person singular or plural of the present subjunctive, and the different parts of the Gerundive.

Rule II

Adjectives, participles, and pronouns, whether belonging to the subject or the predicate, agree in gender, number, and case with the noun or the pronoun to which they refer; as, *Pulvis unus*—One powder; *Uncia una*—One ounce; *Sevum Præparatum*—Prepared suet.

Rule III

The relative must agree with its antecedent in gender, number, and person; as, *Syrupus qui optimus est*—The syrup which is best; *Mistura quæ bona est*—The mixture which is good; *Medicamentum quod neglectum est*—The medicine which has been neglected.

Rule IV

If a verb has more than one subject the verb must be put in the plural number; as, *Pilula et mistura capiantur*—The pill and mixture are to be taken.

Rule V

A participle governs the same case as the verb to which it belongs; as, *Augendo quantitatem*—By increasing the quantity.

Rule VI

The Genitive case primarily signifies the class to which a thing belongs; therefore—

(*a*) It depends on another noun as a notion which it qualifies or determines; as, *pulveris granum*—a grain of powder.

(*b*) Or it is used to signify the whole from which a part is taken; as, *nimium doloris*—too much (of) pain.

(*c*) Adverbs of quantity, time, place, etc., govern the Partitive Genitive; as, *satis aquæ*—enough (of) water.

(*d*) Adjectives of plenty or want govern a Genitive or Ablative; as, *dives quininæ*—rich in quinine; *dives aqua*—rich in water.

Rule VII

Dative.—The sign of the Dative case is *to* or *for*.

(*a*) Adjectives which imply likeness or unlikeness, advantage or disadvantage, etc., govern the Dative; as, *ceræ similis*—like to wax.

(*b*) Verbs of giving or imparting, etc., govern the Dative of the indirect object as well as the Accusative of the direct object; *contusam liquori redde*—return the bruised (substance) to the liquor.

Rule VIII

Accusative.—The Accusative was originally used to mark the immediate object of an action.

(*a*) Transitive verbs in the active voice generally govern the Accusative case; as, *citratem calcis lava*—wash the citrate of lime.

(*b*) The following prepositions govern the Accusative:

Ad ....To, at, for.	*Inter* ....Between, among.
Adversum, adversus ....Against, towards.	*Ob* ....On account of.
Ante ....Before.	*Per* ....Through, by.
Apud ......At, with.	*Pone* ....Behind.
Circum .....Around.	*Post* ....After.
Contra .....Against.	*Prope* ......Near.
Extra ......Outside.	*Secundum* ...According to.
Infra ......Below.	*Supra* ......Above.

(*c*) The following prepositions govern the Ablative as well as the Accusative:

In (ac.) Into; (ab.) in.	*Subter* (ac. and ab.) Under.
Sub (ac.) Under; (ab.) near.	

Rule IX

The Ablative received its name because it signifies ablation or separation, the sign of which is *from*.

(*a*) Cause, manner, means, instrument, time when, and place where, are put in the Ablative; as, *balneo arenæ*—in a bath of sand.

(*b*) *Opus* and *usus* are followed by an Ablative; as, *cibo opus est nobis*—we have need of food.

(*c*) The definite answer to the questions "when" or "how" is expressed by a noun or pronoun and a participle in

the Ablative case, and is called the Ablative absolute; as, *liquoribus omnibus mixtis*—all the liquors having been mixed.

The following prepositions govern the Ablative:

A, ab, abs ... Away from, by.
Cum .... With.
De .... Down from, of, about.
E, ex .... Out of, from, after.
Præ ... Before, because of.
Pro .... For, before, according to.
Sine .... Without.

(*d*) *Utor, abutor*, and a few other verbs govern the Ablative; as, *utatur sequenti*—let him use the following.

Rule X

The Imperative mood is used to express requests or commands; as, *Recipe*—Take (thou).

The Present Subjunctive mood is often used instead of the Imperative; as, *fiat mistura*—let the mixture be made.

LATIN WORDS AND PHRASES MOST FREQUENTLY USED IN PRESCRIPTIONS, BRIEFLY EXPLAINED.*

Aa, Ana (*Greek preposition*). Of each.
A, ab (*prep.*). By or from (*governs abl.*).
Ad 3tiam vicem—Ad tertiam vicem. For three times.
Ad lib.—Ad libitum (*ac., s., libitus-i. Rule* viii.). At pleasure.
Add.—Adde (*im. m., Addo, -didi, -ditum, -ere*). Add.
Admov.—Admove (*im. m., Admoveo, -vi, -tum, -ere*). Apply.
Æger, ægra, ægrum (*adj.*). Sick. (The patient.)
Albus (*-us, -a, -um, adj.*). White.
A.H., Alternis Horis (*ab. pl. Rule* ix.). Every other hour.
Alvo Adst.—Alvo Adstrictâ. The bowels being confined.
Alvus (*-i, n. f.*). The bowels.
Amplus (*-us, -a, -um, adj.*). Large.
App.—Applicandum (*-us, -a, -um, gerundive*). To be applied.

* Abbreviations Used.—*ab.*, or *abl.*, ablative; *ac.*, accusative; *ad.* or *adj.*, adjective; *adv.*, adverb; *conj.*, conjunction; *f.*, feminine *gen.*, genitive; *im.*, or *imp.*, imperative; *indec.*, indeclinable; *indef.* indefinite; *irr.*, irregular; *m.*, or *masc.*, masculine; *m.*, or *mo.* mood; *n.*, or *no.*, noun; *nom.*, or *no.*, nominative; *num.*, numeral *neu.*, neuter; *pas.*, passive; *part.*, participle; *p.*, *pr.*, or *pres.* present; *pl.*, plural; *prep.*, preposition; *pron.*, pronoun; *s.* singular; *sub.*, subjunctive; *t.*, tense; *tr.*, transitive; *v.*, verb.

Aq.—Aqua (*-æ, n. f.*). Water.
Aq. Bull.—Aqua Bulliens (*-entis, adj.*). Boiling water.
,, **Dest.**—Aqua Destillata (*-us, -a, -um, adj.*). Distilled water.
,, **Ferv.**—Aqua Fervens (*-entis, adj.*). Hot water.
,, **Steril.**—Aqua Sterilisata (*-us, -a, -um, adj.*). Sterilized water.
Auris (*-is, n. f.*). The ear.
Aut (*conj.*). Or.
Balneum (*-ei, n. neu.*). A bath.
Bene (*adv.*). Well.
Bibo (*bibere, v. 3rd conj.*). To drink.
B.I.D.—Bis in dies (*adv.*). Twice a day.
B.P. or **Ph. B.**—Pharmacopœia Britannica, British Pharmacopœia.
Brachium (*-ii, n. neu.*). The arm.
C.—Cum (*prep. gov. abl. See Rule* ix.). With.
Calidus (*-us, -a, -um, adj.*). Warm.
Calor (*-oris, n. masc.*). Heat.
Capio (See **Cpt.**). To take.
Caps. dur.—Capsula (*-æ*) dura (*-us, -a, -um*). A hard capsule.
Caps. moll.—Capsula (*-æ*) molle (*-is, -e*). A soft capsule.
Caput (*-itis, n. neu.*). The head.
Cataplasma (*-atis, n. neu.*). A poultice.
Charta (*-æ, n. f.*). A powder or a paper.
Cibus (*-i, n. masc.*). Food.
Circa (*prep. gov. ac.*). Around.
Coch.—Cochlear, Cochleare, or Cochlearium (*n. neu.*). A spoonful.
Coch. Amp.—Cochlear (*-aris*) Amplum (*-us, -a, -um, adj.*). A table-spoonful.
,, **Mag.**—Cochlear (*-aris*) Magnum (*-us, -a, -um, adj.*). A large spoonful; or a table-spoonful.
,, **Med.**—Cochlear (*-aris*) Medium or Modicum (*-us, -a, -um, adj.*). A dessert-spoonful.
,, **Min.**—Cochlear (*-aris*) Minimum (*-us, -a, -um, adj.*). A small spoonful; or a tea-spoonful.
,, **Parv.**—Cochlear (*-aris*) Parvum (*-us, -a, -um, adj.*). A tea-spoonful.
Cochleat.—Cochleatim (*adv.*). By spoonfuls.
Cœna (*-æ, n. f.*). Supper.
Collun.—Collunarium (*-ii, n. neu.*). A nasal wash.

Collut.—Collutorium (*-ii*, *n. neu.*). A mouth-wash.
Collyr.—Collyrium (*-ii*, *n. neu.*). An eye-wash.
Colo (*-avi*, *-atum*, *-are*, *v. a.*). To strain.
Co.—Compositus (*-us*, *-a*, *-um*, *adj.*). Compound.
Comp.—Compositus (*-us*, *-a*, *-um*, *part.*). Compounded.
Confectio (*-onis*, *n. f.*). A confection or electuary.
Cong.—Congius (*-ii*, *n. masc.*). A gallon.
Coq.—Coque (*coquo*, *-xi*, *-ctum*, *-ere*, *v.*, *im. m.*). Boil.
Cpt.—Capiat (*pr. sub.*, *3rd per. s.*, *capio*, *cepi*, *captum*, *capere*. *Rule* x.). Let the patient take.
Cras (*adv.*). To-morrow.
Crus (*cruris*, *n. neu.*). The leg.
Cuj.—Cujus (*gen. s. of qui*, *quæ*, *quod*). Of which.
Cum (*prep. gov. abl.*). With.
Cyath.—Cyathus (*-i*, *n. masc.*). A glass.
C. Vinar.—Cyathus Vinarius. A wine-glass.
D.—Dosis (*dosis*, *n. f.*). A dose.
Da. —Da. (*do*, *dedi*, *datum*, *dare*, *imp. m.*) Give;
Det. —Detur. (*pres. sub.*, *3rd per. s.*) Let it be given.
Decoctum (*-i*, *n. neu.*). A decoction.
Decub.—Decubitus (*-us*, *-a*, *-um*, *part.*). Lying down.
De d. —De die (*es*, *-ei*, *n. masc. ab. s.* *Rule* ix.) From day
in d. —in diem. (*Rule* viii.) to day.
Dej. —Dejectiones (*-onum*, *n. pl.*) Stools, or motions of
Alv. —Alvi (*-i*, *n. f. gen. s.*) the bowel.
Dens (*dentis*, *n. masc.*). A tooth.
Dexter (*-tra*, *-trum*, *adj.*). Right.
Dieb. —Diebus (*-es*, *-ei*, *n. ab. pl.* *Rule* ix.) Every
alt. —Alternis (*-us*, *-a*, *-um*, *adj. pl. ab. m.* *Rule* ii.) other day.
Digitus (*-i.*, *n. m.*). A finger.
Dim.—Dimidius (*-us*, *-a*, *-um*, *adj.*). One half.
Div.—Divide (*-do*, *-visi*, *-visum*, *-dere*, *im. m.*). Divide.
Div. —Dividatur (*-vido*, *-visi*, *-sum*, *-ere*, *v. 3rd per. s. pres. pas. sub.*) Let it be divided
in —in (*prep. gov. partes*. *Rule* viii. *c.*) into
p. —partes (*n. ac. pl. gov. by in*) parts
æq. —æquales (*adj.*, *agreeing with partes*) equal.
Dolor (*-oris*, *n. masc.*). Pain.
Donec (*conj.*). Until.
Durant. —Durante (*-ans*, *-antis*, *part.*) While the pain
Dolor. —Dolore (*-oris*, *n. masc.*) lasts.

Dos.—Dosis (*-is, accusative dosin, n. f.*). A dose.
Drachma (*-æ, n. f.*). A drachm.
Dulcis (*-is, -is, -e, adj.*). Sweet.
Dum (*adv.*). Whilst.
Duo (*duo, -æ, -o, adj.*). Two.
E or **Ex** (*prep. gov. abl.*). Out of.
Effervescentia (*-æ, n. f.*). Effervescence.
Ejusd.—Ejusdem (*idem, eadem, idem, gen. s.*). Of the same.
Emesis (*-is, n. f.*). Vomiting.
Emplastrum (*-tri, n. neu.*). A plaster.
Enema (*-atis, n. neu.*). An enema or clyster.
Et (*conj.*). And.
Extractum (*-i, n. neu.*). An extract.
F.—Fac. (*facio, feci, factum, facere, imp. m., 2nd per. s.*). Make.
Febris (*-is, n. f.*). Fever.
Fer.—Ferrum (*-i, n. neu.*). Iron.
Ferv.—Fervens (*-ens, -entis, adj.*). Hot.
Flatus (*-us, n. masc.*). Flatulence.
Flavus (*-us, -a, -um, adj.*). Yellow.
Flos (*-oris, n. masc.*). A flower.
Fol.—Folium (*-ii, n. neu.*). A leaf.
Frigidus (*-a, -um, adj.*). Cold.
Frequenter (*adv.*). Frequently.
Ft.—Fiat (*fio, factus, fieri, pres. sub. 3rd s.*). Let it be made.
Ft.—Fiant (,, ,, ,, ,, ,, ,, *pl.*). Let them be made.
Garg.—Gargarisma (*-matis, n. neu.*). A gargle.
Genu (*-us, n. neu.*). The knee.
Gradatim (*adv.*). By degrees.
Gr.—Granum (*-i, n. neu.*). A grain.
Gtt.—Gutta (*-æ, n. f.*). A drop.
Guttat.—Guttatim (*adv.*). By drops.
H.—Hora (*-æ, n. f.*). An hour.
Haust.—Haustus (*-us, n. masc.*). A draught.
Hebdomas (*-adis, n. f.*). A week.
Heri (*adv.*). Yesterday.
Hodie (*adv.*). To-day.
Hora (*-æ, n. f.*). An hour.
H.S.S.—Hora Somni Sumendum. To be taken at bed-hour.
Idem (*idem, eadem, idem, pron.*). The same.
In (*prep. gov. abl. or ac.*). In or into.
In d.—In-dies (*adv.*). From day to day, or daily.

Infra (*prep. gov. ac.*). Below.
Infrico (*-cui, -ctum, and -catum, -are*). To rub in.
Infusum (*-i, n. neu.*). An infusion.
Inhalatio (*onis, n. f.*). An inhalation.
Injectio (*-onis, n. f.*). An injection.
Insufflatio (*-onis, n. f.*). A snuff.
Intime (*adv.*). Thoroughly.
Jecur (*jecoris, n. neu.*). The liver.
Latus (*-eris, n. neu.*). The side.
Laxativus (*-us, -a, -um, adj.*). Laxative.
Levis (*-is, -is, -e, adj.*). Light.
Libra (*-æ, n. f.*). A pound.
Linctus (*-i, n. masc.*). A linctus.
Lin.—Linimentum (*-i, n. neu.*). A liniment.
Liquidus (*-us, -a, -um, adj.*). Liquid.
Liquor (*-oris, n. masc.*). A liquid.
Lotio (*-onis, n. f.*). A lotion.
Macero (*-avi, -atum, -are*). To macerate.
Mag.—Magnus (*-us, -a, -um, adj.*). Large.
Mane (*indec. neu. n.—used adverbially*). In the morning.
Mane Primo (*adv.*). Very early in the morning.
M.—Massa (*-æ, n. f.*).—A mass.
M.—Misce (*misceo, miscui, mistum, miscere, pres. imper.*). Mix
M. or **Min.**—Minimum (*-i, n. neu.*). A minim.
Med.—Medicamentum (*-i, n. neu.*). A medicine.
Medius (*-us, -a, -um, adj.*). Middle.
Meridies (*-ei, n. masc.*). Mid-day or noon.
Mist.—Mistura (*-æ, n. f.*). A mixture.
Mitte (*mitto, misi, missum, mittere, 2nd per. s. pres. imper.*). Send.
Modicus (*-us, -a, -um, adj.*). Middle-sized.
Mol.—Mollis (*-e, adj.*). Soft.
More dict.—More dicto (*more, mos, -ris, n. masc.*; *dicto, dico, -xi, -ctum, -ere, part.*). In the manner directed.
M.D.U.—More dicto utendum (*utendus, -a, -um*; *gerundive of utor*). To be used as directed.
More Sol.—More solito (*solitus sum, solere, v. neu. pas.*). To be accustomed. In the usual manner.
Nebula (*-æ. n. f.*). A nasal spray.
Nig.—Niger (*-ra, -rum, adj.*). Black.
Nisi (*conj.*). Unless.
Nox (*noctis, n. f.*). Night.

N.P.—Nomen Proprium. The proper name.
Nux (*nucis, n. f.*). A nut.
Oblatum (*-i, n. neu.*). A cachet.
Octarius (*-ii, n. masc.*). A pint.
Oculus (*-i, n. masc.*). An eye.
Oleum (*-ei, n. neu.*). Oil.
Om.—Omnis (*-is, -is, -e, adj.*). All; every.
Omn. Hor.—Omni Hora (*-æ, n. f.*). Every hour.
Omn. Quadr. Hor.—Omni Quadrante Horæ (*Quadrans, -tis, ab. f.*). Every quarter of an hour.
Ope (*ops, opis, n. f. ab. s.*). *Rule* ix. (*a*). By the aid of.
Optimus (*-us, -a, -um, adj.*). Best.
Opus (*indec. n. neu.*). Need or occasion.
P.Æ.—Partes Æquales (*-is, -is, -e, adj.*). Equal parts.
Pars (*-tis, n. f.*). A part.
Parvulus (*-us, -a, -um, adj.*). Very little.
Parvus (*-us, -a, -um, adj.*). Little; small.
Pasta (*-æ, n. f.*). A paste.
Pastillus (*-i, n. masc.*). A pastille.
Paul.—Paululus (*-us, -a, -um, adj.*). Little.
Pectus (*-oris, n. neu.*). The breast.
Per (*prep. gov. ac.*). Through.
Pes (*pedis, n. masc.*). The foot.
Pessus (*-i, n. masc.*). A pessary.
Pigmentum (*-i, n. neu.*). A paint.
Pil.—Pilula (*-æ, n. f.*). A pill.
Pocul.—Poculum (*-i, n. neu.*). A cup; a little cup.
Pollex (*-icis, n. masc.*). The thumb.
Pone (*prep. gov. ac.*). Behind.
Post (*prep. gov. ac.*). After.
Postea (*adv.*). Afterwards.
Post singulas dejectiones liquidas. After each loose motion.
P.P.A.—Phiala prius agitata (*ablative absolute*). The bottle having been first shaken.
Prandium (*-ii, n. neu.*). Dinner.
Primus (*-us, -a, -um, adj.*). First.
P.R.N.—Pro re nata (*adverbial phrase*). Occasionally, or according to circumstances.
Pro (*prep. gov. ab.*). Before.
Pulmo (*-onis, n. masc.*). A lung.
Pulv.—Pulvis (*-veris, n. masc.*). A powder.

Pulv. consper.—Pulvis conspersus. A dusting powder.
Q.Q.—Quaque *f.* or Quoque *masc.* (*quisque, quæque, quodque, abl. s. indef. pron.*). Each or every.
Q.S. —Quantum (*adv.*) —Sufficiat (*sufficio, -feci, -fectum, -ere*) As much as is sufficient.
Quaque Hora (*abl. of quisque, quæqüe, quodque, pron.*). Each hour.
Quartus (*-us, -a, -um, adj.*). Fourth.
Quater (*adv.*). Four times.
Quibus (*qui, quæ, quod, rel. pron. abl. pl.*). From which.
Quintus (*-us, -a, -um, adj.*). Fifth.
Quor.—Quorum (*qui, quæ, quod, pron.*). Of which.
Quotidie (*adv.*). Daily.
℞.—Recipe (*recipio, recepi, receptum, recipere, im. m.*). Take thou.
Rad.—Radix (*-icis, n. f.*). A root.
Rec.—Recens (*-ens, -ens, -ens, adj.*). Fresh.
Rept. —Repetatur (*repeto, -ivi, -itum, -ere, sub. m. 3rd s.*) Let it be repeated. —Repetantur (*3rd pl.*) Let them be repeated.
S.A.—Secundum Artem (*secundum, prep.; ars, artis, n. f.*). According to Art.
Sæpe (*adv.*). Often.
Scrupulus (*-i, n. masc.*). A scruple.
Secundus (*-us, -a, -um, adj.*). Second.
Sem.—Semen (*-inis, n. neu.*). Seed.
Semiuncia (*-æ, n. f.*). A half-ounce.
Separatim (*adv.*). Separately.
Sesquih.—Sesquihora (*sesquihora, -æ, n. f.*). An hour and a half.
Sextus (*-us, -a, -um, adj.*). Sixth.
Si (*conj.*). If.
Sig.—Signa (*signo, -avi, -atum, -are, im. m.*). Mark thou.
Simul (*adv.*). Together; at the same time.
Sine (*prep.*). Without (*gov. abl.*).
Sing.—Singulorum (*singulus, -a, -um, adj.*). Of each.
Si op. sit—Si opus sit. If necessary.
Sit (*sum, fui, esse, pr. sub.*). Let it be.
S.N.—Secundum Naturam (*-a, -æ, n. f.*). According to nature.
Solve (*solvo, solvi, solutum, solvere*). Dissolve.
Somnus (*-i, n. masc.*). Sleep.

Spt.—Spiritus (*-us, n. masc.*). Spirit.
Ss.—Semis (*-is, -issis, n. masc.*). A half.
S.S.—Statim Sumendum. To be taken immediately.
St.—Sumat (*sumo, sumpsi, sumptum, sumere, pr. sub.*). Let him take.
Stat.—Statim (*adv.*). Immediately.
Sub (*prep. gov. ac. or abl.*). Under.
Subinde (*adv.*). Frequently.
Suc.—Succus (*-i, n. masc.*). Juice.
Sum.—Sume (*sumo, sumpsi, sumptum, sumere, im. m.*). Take.
Super (*prep. gov. ac. or abl.*). Over.
Supra (*prep. gov. ac.*). Above.
Syrupus (*-i, n. masc.*). Syrup.
Tabella (*-æ, n. f.*). A tablet.
Talis (*talis, talis, tale, adj.*). Such.
Ter (*adv.*). Thrice.
Tere (*tero, trivi, tritum, terere, im. m.*). Rub.
Tertius (*-us, -a, -um, adj.*). Third.
Thorax (*-acis, n. masc.*). The chest.
Tr. or **Tinct.**—Tinctura (*-æ, n. f.*). A tincture.
Trit.—Tritura (*trituro, triturate, im. m.*). Triturate; grind.
Trochiscus (*-i, n. m.*). A lozenge.
Tussis (*-is, n. f.*). A cough.
Una (*adv.*). Together.
Uncia (*-æ, n. f.*). An ounce.
Ungt.—Unguentum (*-i, n. neu.*). An ointment.
Unus (*-a, -um, adj.*). One.
Ut Dict.—Ut Dictum. As directed.
Utend.—Utendum (*-us, -a, -um, gerundive*). To be used.
Vac. Ven.—Vacuo Ventriculo (*adj. and n., abl. s.*). *Rule* ix. (*a*). On an empty stomach.
Vel (*conj.*). Or.
Vena (*-æ, n. f.*). A vein.
Venenum (*-i, n. neu.*). Poison.
Ver.—Verus (*-us, -a, -um, adj.*). Genuine.
Vesicatorius (*-us, -a, -um, adj.*). Blistering.
Vesp.—Vesper (*-eris, n. masc.*). The evening.
Vices (*n. f. defective*). Time.
Viginti (*numeral adj. indec.*). Twenty.
Vinum (*-i, n. neu.*). Wine.
Virus (*-i, n. neu.*). Poison.
Vitellus (*-i, n. masc.*). Yolk (i.e. of egg).

Mr. R. T. Thompson

℞. Tr. Quin. ʒi.
Tr. Nuc. Vom. ʒi.
Syr. Aromat. ʒiss.
Inf. Quass. ad ℥viij. m.
Ft. Mist. Capt. Coch. mag. ter die ante cib.

℞ Papain gr. ii.
Bism. Carb. gr. v.
Sodii Bicarb. gr. xv.
Mag. Carb. Pon. gr. v.
Menthol gr. ss. m.
Ft. Cachet mitte tales xxiv
St. i hor. 1. post cib. ter die.

℞. Ext. Aloes gr. iss.
Ext. Casc Sag. sicc. gr. i.
Glycer. Trag. q. s.
ut ft. pil. mitte xii. st. i om. n. h. s.
5/10/14.

SPECIMEN PRESCRIPTION

The preceding recipe may be taken as a sample of a physician's prescription, and the student will do well to study carefully the various contractions and compare them with the Latin words which they represent.

Recipe
Tincturæ Quininæ, unciam.
Tincturæ Nucis Vomicæ, drachmam.
Syrupi Aromatici, unciam cum semisse.
Infusi Quassiæ, ad uncias octō. *Misce.*
Fiat Mistura. Capiat cochlearium magnum ter die ante cibos.

Recipe
Papain, grana duo.
Bismuthi Carbonatis, grana quinque.
Sodii Bicarbonatis, grana quinquedecim.
Magnesii Carbonatis Ponderosi, grana quinque.
Menthol, semigranum. *Misce.*
Fiat cachet. Mitte tales viginti et quatuor. Sumat unam hora una post cibos ter die.

Recipe
Extracti Aloes, granum cum semisse.
Extracti Cascaræ Sagradæ Sicci, granum.
Glycerini Tragacanthæ quantum sufficiat ut fiat pilula. Mitte tales duodecim. Sumat unam omne nocte hora somni.

Take of
Tincture of Quinine, one ounce.
Tincture of Nux Vomica, one drachm.
Aromatic Syrup, one ounce and a half.
Infusion of Quassia, to eight ounces. Mix.
Make a mixture. One tablespoonful to be taken three times daily before meals.

Take of
Papain, two grains.
Carbonate of Bismuth, five grains.
Bicarbonate of Sodium, fifteen grains.
Heavy Carbonate of Magnesium, five grains.
Menthol, half a grain. Mix.
Make a cachet. Send twenty-four such. One to be taken one hour after meals three times daily.

Take of
Extract of Aloes, one grain and half.
Dry Extract of Cascara Sagrada, one grain.
Glycerin of Tragacanth a sufficient quantity to make a pill. Send twelve such. One to be taken every night at bedtime.

The Dangerous Drugs Act requires the following details on a prescription before it may be dispensed :

1. The prescriber's postal address.
2. The date in his own writing.
3. The name and address of the patient.
4. The total amount of the Dangerous Drug to be supplied, or the amount of the preparation, if the drug is contained in the B.P. or B.P.C.
5. The prescriber's *usual* signature with surname in full.
6. If the prescriber wishes the prescription to be repeated, it must be specified on it and the interval or intervals stated. A prescription cannot be repeated more than twice—i.e. dispensed three times in all.

INCOMPATIBILITY

Incompatibility may be defined as any reaction occurring between the ingredients of a preparation when mixed, resulting in a chemical, physical, or therapeutical change. The change may, in some cases, be intentional on the part of the prescriber, and the dispenser will generally recognize this, but he must always be on his guard for that type of incompatibility which prevents the prescriber's intention from being carried out, and particularly the type which may lead to fatal results if the prescription is dispensed as written. An understanding of compatibility demands a knowledge of the chemistry of drug constituents and pharmaceutical processes.

Incompatibility may be classified as follows :

1. **Intentional incompatibility,** when the prescriber intends that certain ingredients shall react to produce a third, as when citric acid and potassium bicarbonate are prescribed together in a mixture. Potassium citrate is formed in a solution well charged with carbon dioxide. Ferrous sulphate and potassium or sodium carbonate are often prescribed together with the object of producing fresh ferrous carbonate (see Pil. Ferri Carb. B.P.). The following are well-known gargles :

℞. *Sod. Salicyl.* ʒij.
Pot. Bicarb. ʒij.
Liquor Ferri Perchlor. ʒij.
Aq. Menth. Pip. *ad* ℥viij.

When these ingredients are mixed, a very brisk effervescence occurs with the production of a cherry-red solution.

℞. *Pot. Chlorat.* ℈i.
Acid. Hydrochlor. ʒss.
Aquam ad ℥vi.

Misce et fiat gargar. chlorinat.

Here it is intended that the ingredients shall interact and produce a gaseous mixture of chlorine and chlorine peroxide (the two together are often known as Euchlorine), which is to be dissolved in the water, and the dispenser must manipulate the preparation so as to produce that result. This can only be done by pouring the acid on to the powdered potassium chlorate in the bottle, and allowing it to stand for about ½ hour. If the two are diluted with water very little interaction takes place.

2. **Unintentional incompatibility,** when, no matter how the ingredients are mixed, a change occurs which was not intended by the prescriber. This type may be sub-divided into those changes which are:

(*a*) *Not dangerous, and result in no change of therapeutic activity.* Thus, when a resinous tincture such as those of guaiacum, myrrh, podophyllum are prescribed in mixture, a precipitate of resin is thrown down. Such a precipitate is usually suspended with mucilage, and no therapeutic change results. When alkalies, such as borax, are prescribed with Acid Infusion of Rose, a dirty green-blue mixture results which, though not dangerous, is very unsightly, and was certainly not intended by the prescriber, who wanted a bright red preparation.

(*b*) *Not dangerous, but inactivation occurs.* Thus pancreatin will become inactive very quickly if dispensed in an acid solution and, *vice versa*, the following are quickly inactivated in alkaline solution: adrenaline, physostigmine salicylate, pituitrin, insulin, apomorphine hydrochloride pepsin.

(*c*) *Dangerous, but can be manipulated by the dispenser with the production of a safe preparation of full activity.* A very common one is the prescribing together of Spirit of Nitrous Ether and potassium iodide. The former contains a varying quantity of free nitrous acid (which increases with the age of the preparation) which, interacting with the Iodine, produces free Iodine, which may be dangerous to the patient.

If, however, the Spirit be made neutral or slightly alkaline with sodium bicarbonate, no such reaction will occur. For the same reason, phenazone will usually give a green colour with Spirit of Nitrous Ether, which change can be similarly prevented.

(*d*) *Dangerous, and cannot be prevented.* This is, of course, the most important type, and the dispenser should refuse to dispense.

Probably the most likely example which may occur is when a preparation containing a toxic alkaloid is prescribed in a mixture with an ingredient which is an alkaloidal precipitant, with the result that a precipitate of the free alkaloid collects at the bottom of the mixture. There is then the possibility (and actual cases have been known) of the patient not shaking the bottle before measuring a dose and receiving a fatal quantity of alkaloid when taking the last dose. The student *must* remember that the following are alkaloidal precipitants and must not be dispensed in mixtures containing toxic alkaloids:

Alkalies and preparations containing alkalies, such as Aromatic Spirit of Ammonia.

Tannins and preparations containing tannins, such as Syrup of Virginian Prune.

Solutions of double iodides, such as mercuric potassium iodide, arsenious and mercuric iodide (Donovan's Solution), and substances which produce such double iodides as mercuric chloride and potassium iodide. These double iodides form a precipitate of a compound containing both the double iodide and the alkaloid, and are thus doubly toxic. Conversely, a relatively non-toxic alkaloid like quinine will form a toxic precipitate with these double iodides. The following mixture forms such a precipitate owing to the alkaloids in the Infusion of Calumba.

℞. *Hydrarg. Perchlor.* gr. i.
Potass. Iodid. ʒij.
Inf. Calumb. *ad* ℥viii.

If the Inf. Calumb. be replaced by Inf. Gent. Co. or Inf. Quass., no precipitation will occur.

When the dispenser considers that the ingredients as prescribed would constitute on mixing such incompatibility as to be dangerous to the patient or would result in the

inactivation of the preparation, and that he cannot prevent such changes, it is his duty to communicate with the prescriber and ask for instructions.

The following is a list of incompatibles :

Acacia, with strong alcohol, borax, lead subacetate, ferric salts.

Acetylsalicylic acid (aspirin), with water (or moisture).

Adrenaline : Very liable to oxidize, particularly if in alkaline solution. All solutions should be kept slightly on the acid side of neutrality with a little hydrochloric acid. Oxidizing agents inactivate it, such as ferric salts. Changes in colour on oxidation to pink, red, brown.

Alkaloidal salts, with alkalies, tannins, double iodides.

Apomorphine (as for adrenaline). Changes on oxidation to a green colour.

Chloral Hydrate : with alkaline carbonates and hydroxides it forms chloroform on standing.

Chloramine T, with soap.

Chlorates : Explosive mixture if mixed dry with reducing agents. Should always be prescribed *per se* or in solution.

Gelatin : Solutions are coagulated with solutions of tannins, formaldehyde, potassium dichromate.

Glyceryl trinitrate : Liquor Glyceryl Trinitrat., when mixed with water, throws down an oily deposit of glyceryl trinitrate.

Iron salts, with alkaline carbonates, hydroxides, tannin, acacia. The red colour in Acid Infusion of Roses is turned bluish-green.

Soluble lead salts, with alkaline carbonates, hydroxides, sulphates, chlorides, bromides, iodides, tannins.

Liquorice, Extracts of, with acids give a precipitate.

Menthol will liquefy when mixed with any of the following, and is often intentionally so prescribed : camphor, chloral hydrate, thymol, phenol, resorcin.

Mercuric chloride, with alkaline carbonates, hydroxides, hypophosphites, alkaloids, tannins.

Mercurous chloride : When dispensed in pill form, acacia must be avoided, as the two form a cement.

Pancreatin, inactivated by acids and strong alcohol.

Pepsin, inactivated by alkalies and strong alcohol.

Phenazone, with nitrous acid (Spirit of Nitrous Ether, see p. 272).

Potassium permanganate: A very powerful oxidizing agent. When dispensed in pill form, should be massed with wool fat and kaolin.

Salicylates, with acids give a white precipitate of salicylic acid.

Silver nitrate, with chlorides (tap-water), bromides, iodides, carbonates, hydroxides and light.

Spirit of Nitrous Ether (nitrous acid), with iodides, bromides, phenazone, salicylates, tannins.

Strophanthin and Tincture of Strophanthus, with water, quickly become inactivated owing to hydrolysis.

Tannins, with gelatin, alkaloids, iron salts.

CHAPTER XVI

MATERIA MEDICA OF THE BRITISH PHARMACOPŒIA

PHARMACOPŒIAL PREPARATIONS

THE British Pharmacopœia contains many groups of preparations; these are known as the official Galenicals. The term is derived from one of the early fathers in our art (Galen, A.D. 130–200), and it is employed in contradistinction to the extemporaneous or Magistral preparations (physicians' prescriptions), whose formulæ are written extemporarily by a magister or master of his profession. These groups of the B.P. preparations should be studied after the student has grasped the details of the official remedies which immediately follow them in the present volume, but they may be glanced at with advantage from time to time during the period of study of those details when a member of the group turns up under the heading of an official drug. This summary includes the new products introduced by the 1st, 2nd, 3rd, and 4th Addenda to the Pharmacopœia.

The Aceta or Vinegars are galenicals in which Acetic Acid is the solvent. Only one is official:

Acetum Scillæ—Contains approximately 10% w/v of the active principles of squill. Bruised squill macerated in dilute acetic acid for 7 days, pressed, filtered.

Antitoxins.—The following are official :

Antitoxinum Diphthericum (Diphtheria Antitoxin) (also p. 150)—A serum or preparation from a serum, containing the antitoxic globulins which have the specific power of neutralizing the toxin formed by *Corynebacterium diphtheriæ*. *Storage*—Should be stored at as low a temperature as possible above its freezing point. *Dose*—By injection : prophylactic, 500 to 1000 units ; therapeutic, 10,000 to 20,000 units.

Antitoxinum Œdematiens (Gas Gangrene Antitoxin) (Œdematiens)—A serum or a serum preparation, containing the antitoxic globulins, which have the specific power of neutralizing the toxin formed by *Clostridium œdematiens*. The serum may be used in the liquid form or may be dried. If in the liquid form an antiseptic may be added. *Storage*—Should be stored at as low a temperature as possible above its freezing point. *Dose*—By injection : prophylactic, 20,000 units ; therapeutic, 50,000 to 100,000 units.

Antitoxinum Staphylococcicum (Staphylococcus Antitoxin) —A serum or preparation from a serum, containing the antitoxic globulins which have the specific power of neutralizing the toxin formed by certain strains of Staphylococcus. The serum may be used in the liquid form or may be dried. If in the liquid form an antiseptic may be added. *Storage*—Should be stored at as low a temperature as possible above its freezing point. *Dose*—By injection : 5000 to 20,000 units.

Antitoxinum Vibriosepticum (Gas Gangrene Antitoxin) (Vibrion Septique)—A serum or a preparation from a serum, containing the antitoxic globulins which have the specific power of neutralizing the toxin formed by the Clostridium, commonly known as Vibrion Septique. The serum may be used in the liquid form or may be dried. An antiseptic may be added to the liquid forms. *Storage*—Should be stored at as low a temperature as possible above its freezing point. *Dose*—By injection : prophylactic, 5000 units ; therapeutic, 10,000 to 20,000 units.

Serum Antidysentericum (Shiga) (Antidysentery Serum (Shiga))—A serum containing the immune substances, which have a specific therapeutic action when injected into persons infected by *Bacillus dysenteriæ* (Shiga). Serum may be used in liquid form or dried. The separated globulins may be used dried or in solution. An anti-

septic may be added to the liquid forms. *Storage*—Should be stored at as low a temperature as possible above its freezing point. *Dose*—By injection; 4000–10,000 units.

Serum Antipneumococcicum I (Antipneumococcus Serum) (Type I)—Antipneumococcus Serum (Type I) is a serum or preparation of a serum, containing the immune substances, which have a specific therapeutic action, when injected into persons suffering from certain diseases due to *Diplococcus pneumoniæ* (Type I) The serum may be used in the liquid form or may be dried. An antiseptic may be added to the liquid forms. *Storage*—Should be kept at as low a temperature as possible above its freezing point. *Dose*—By intravenous injection, 50,000 to 150,000 units.

Serum Antipneumococcicum II (Antipneumococcus Serum) (Type II)—A similar preparation to the above, with the modification that strains of Diplococcus pneumoniæ (Type II) are used in the preparation and assay.

Antitoxinum Tetanicum (Tetanus Antitoxin) (also p. 151)—A serum preparation, containing the antitoxic globulins which have the specific power of neutralizing the toxin formed by *Clostridium tetani*. *Storage*—Should be stored at as low a temperature as possible above its freezing point. *Dose*—By injection: prophylactic, 1000 to 2000 units; therapeutic, 20,000 to 40,000 units.

Antitoxinum Welchii—Gas Gangrene Antitoxin (perfringens) (also p. 151)—A serum preparation, containing the antitoxic globulins which have the specific power of neutralizing the toxin formed by *Clostridium perfringens* (*Bacillus Welchii*). *Storage*—Should be stored at as low a temperature as possible above its freezing point. *Dose*—Prophylactic, 4000 units by injection; therapeutic, 10,000 to 20,000 units by intravenous injection.

Aquæ Aromaticæ (Aromatic Waters) are aqueous solutions of aromatic principles, usually volatile oils, and are used chiefly as vehicles for the administration of other medicaments. Their preparation varies. The following are simple solutions:

Aqua Camphoræ—Obtained by dissolving camphor in a little 90% alcohol, pouring into water and shaking occasionally until dissolved. Strength 1 in 1,000 w/v.

Aqua Chloroformi—Obtained by dissolving chloroform in water. Strength 1 in 400 v/v.

The other aromatic waters may be made by the following alternative methods:

1. **Aquæ Aromaticæ Destillatæ** (Distilled Aromatic Waters)—

   These are prepared by distilling the drug or volatile oil with water. Prepared in this manner, aromatic waters are generally superior in aroma and flavour to those made by other methods. The following distilled waters are official: Aqua Anethi Dest., Aqua Cinnamomi Dest., Aqua Menthæ Piperitæ Dest. *They are only dispensed when the prescriber specifically denotes them as "distilled,"* otherwise those made by one of the following methods may be used.

2. Solution of volatile oil, by either shaking the volatile oil with 500 times its volume of distilled water, allowing to stand and filtering, or by absorbing the volatile oil on powdered talc, kieselguhr, or pulped filter-paper, mixing with 500 times its volume of distilled water and filtering.

3. Dilution from concentrated waters, by diluting these with 39 times their volume (1 in 40) of distilled water.

Aquæ Aromaticæ Concentratæ (Concentrated Aromatic Waters).—These are weak alcoholic solutions of volatile oils, and for use are diluted 1 in 40 with distilled water to produce aromatic waters. They are prepared by dissolving 2 parts of volatile oil in 60 parts of alcohol (90 per cent.), gradually adding distilled water to 100 parts and clarifying by the addition of talc and subsequent filtration.

The following are official:

Aqua Anethi Concentrata.

Aqua Cinnamomi Concentrata.

Aqua Menthæ Piperitæ Concentrata.

Cataplasmata (Poultices).—Only one is official:

Cataplasma Kaolini (Poultice of Kaolin)—Prepared by mixing kaolin and boric acid with glycerin, heating to 120° for one hour, stirring occasionally and allowing to cool.

Then adding a solution of thymol in a mixture of methyl salicylate and oil of peppermint, mixing thoroughly.
A 70 per cent. Sodium Lactate solution replaces the glycerin in the 4th Addendum (a war economy).

Collodium Flexile (Flexible Collodion).—A solution of pyroxylin, colophony and castor oil, alcohol (90 per cent.) and ether. This preparation, when painted on the skin, leaves a flexible protective film.

Confections.—Confections are soft preparations of a pasty consistence, containing a medicament blended with some form of sugar to make its administration more agreeable. They were formerly known as Conserves and Electuaries.

CONFECTIONS.

CONFECTIO.	CONSTITUENTS.	STRENGTH.	DOSE.
Sennæ	Powdered senna, powdered coriander, figs, tamarind and cassia, prunes, extract of liquorice, sucrose, water q.s.	10% of senna.	60 to 120 gr. (4 to 8 gm.).
Sulphuris ..	Sulphur, acid potassium tartrate, tragacanth, syrup, tincture of orange, glycerin.	45% of sulphur.	60 to 120 gr. (4 to 8 gm.).

Elixirs.—These are usually sweet aromatic preparations containing a good proportion of alcohol. The only official one, however, contains little alcohol and is an aromatic preparation of cascara, less bitter than the liquid extract.

Elixir Cascaræ Sagradæ (Elixir of Cascara Sagrada)—It is prepared by exhausting a mixture of cascara, liquorice, light magnesium oxide by maceration and percolation with boiling distilled water, concentrating and incorporating soluble saccharine and an alcoholic solution of oils of coriander and of anise, then adjusting to volume with distilled water. *Dose*—½ to 1 dr.

Emplastra.—Plasters (also p. 205).—These are solid adhesive applications for external use, either for support or as a local means of applying various active remedies. Lead plaster is used as a basis for other official plasters :

Emplastrum Belladonnæ (Plaster of Belladonna)—Belladonna root is exhausted by percolation with a mixture of 7 parts of alcohol (90%) or industrial methylated spirit and 1 part of water. The percolate is evaporated to a firm extract, assayed for total alkaloids, and incorporated in sufficient colophony plaster to produce a plaster containin 0·25% total alkaloids.

Belladonna Plaster may also be made with a rubber basis, provided the same alkaloidal strength is maintained. Any suitable rubber basis may be used.

Emplastrum Cantharidini (Plaster of Cantharidin)—Blistering plaster. Cantharidin 0·2% dissolved in acetone and incorporated in castor oil, yellow beeswax, wool fat.

Emplastrum Colophonii (Plaster of Colophony ; Resin Plaster ; Adhesive Plaster)—Resin, lead plaster, hard soap melted and mixed.

Emplastrum Plumbi (Lead Plaster ; Diachylon)—Lead oxide, olive oil and water, boiled together until the oxide is used up. The mass is then cooled, kneaded under water to get rid of glycerin, and rolled into sticks. It consists chiefly of lead oleate.

Emulsiones (Emulsions).—Details of the preparation of emulsions will be found on page 171. The Second Addendum introduces two emulsions—

Emulsio Olei Morrhuae (Emulsion of Cod Liver Oil). A 50 per cent. o/w emulsion of Cod Liver Oil, sweetened with Saccharin, preserved with Chloroform and flavoured with volatile oil of almonds. Dose 30–60 mins. (2–4 mils). This dose is approximately equivalent to 2000 units of Vit. A, and 200 units of Vit. D.

Emulsio Olei Vitaminati (Emulsion of Vitaminized Oil). A 50 per cent. o/w emulsion of Vitaminized Oil. Otherwise as above. Dose, 30–60 mins (2–4 mils). This dose is approximately equivalent to 2000 units of Vit. A, and 200 units of Vit. D.

Extracta (Extracts).—These are preparations containing the active principles of a drug in a very concentrated form, with the minimum amount of inert matter. The matter may be extracted with either water, alcohol, or a mixture of these, or with ether. In the latter case, the ether is always subsequently evaporated off. The methods of extraction vary, consisting of maceration, percolation, infusion, or decoction.

Concentration of the extractive may proceed until a certain volume is obtained (Liquid Extracts), or until a soft mass results (Soft Extracts), or to dryness (Dry Extracts). In the case of liquid extracts in which water is the solvent, it is necessary to add about 25 per cent. of alcohol (90 per cent.) as a preservative against fermentation and fungoid growth.

The Pharmacopœia permits the use of industrial methylated spirit of equivalent strength to be substituted for alcohol in the preparation of extracts when the process is such that no industrial methylated spirit would be left in the finished product.

Strength of Extracts.—The strength of Liquid Extracts of drugs whose active principles are not of a potent nature is usually adjusted so that one part by weight of the drug produces one part by volume of the finished product (or 1 in 1).

When the drug contains potent active principles and can be assayed, the Liquid Extract is adjusted to a definite percentage of active principle which represents the percentage of active principle in an average sample of the crude drug. Thus, ipecacuanha generally contains about 2 per cent. total alkaloids. Liquid Extract of Ipecacuanha is adjusted to this strength so that the strength is really based upon the same idea as the Liquid Extracts of non-potent drugs (viz. 1 in 1).

The strength of Soft Extracts cannot be adjusted because of the difficulty of finding a suitable diluent. Soft Extracts can consequently vary, but as nearly all the Soft Extracts in the Pharmacopœia are of a non-potent character, such as Extract of Malt and Extract of Gentian or Liquorice, the variation is not a serious matter. (Extract of Cinchona is an exception. It is a Soft Extract, diluted to a definite alkaloidal strength with glycerin.) The strength of dry potent extracts bears no relation to the crude drug, but is based upon the *dosage*, being so adjusted that the maximum dose is *never less* than 1 gr. or 0·06 gm. Various diluents are used to adjust the strength, viz. calcium phosphate, lactose, starch and in the case of extracts from Belladonna and Hyoscyamus—the powdered leaf.

Dosage.—Because of the great variation in the strengths of the various extracts, the doses are correspondingly very irregular, but it is very important that the student should remember the maximum doses, particularly of the potent ones. He should bear in mind that extracts are *the most con-*

centrated type of galenical. The following maximum doses should be specially noted:

1 grain — Ext. Bellad. Sicc., Ext. Colch. Sicc., Ext. Hyoscy. Sicc., Ext. Nuc. Vom. Sicc., Ext. Opii Sicc., Ext. Stramon. Sicc.
1 minim —Ext. Bellad. Liq.
2 minims—Ext. Ipecac. Liq.
3 minims—Ext. Nuc. Vom. Liq.
5 minims—Ext. Colch. Liq.
6 minims—Ext. Hyoscy. Liq.
20 minims—Ext. Ergotæ Liq.

SOFT EXTRACTS

EXTRACTUM.	METHOD.	STRENGTH.	DOSE.
Cinchonæ ..	Macerate and percolate the bark with 90% alcohol. Concentrate, add glycerin, assay and adjust to strength.	10% total alkaloids.	2 to 8 gr. (0·12 to 0·5 gm.).
Fellis Bovini	Evaporate fresh ox bile to ¼ volume. Add alcohol, allow to stand, filter, evaporate filtrate on a water-bath to a firm extract.		5 to 15 gr. (0·3 to 1 gm.).
Gentianæ ..	Infuse Gentian Root with hot water for 2 hours; boil for 15 minutes, strain, evaporate to soft extract.		2 to 8 gr. (0·12 to 0·5 gm.).
Glycyrrhizæ	Macerate and percolate the powdered root with chloroform water. Boil the percolate for 5 minutes, filter, evaporate to soft extract.		10 to 30 gr. (0·6 to 2 gm.).
Malti.. ..	Infuse Malted Barley with water, strain, evaporate under reduced pressure until a viscous product is obtained.		1 to 4 dr. (4 to 16 mils).
Malti cum Oleo Morrhuæ ..	Incorporate Cod-Liver Oil in Extract of Malt.	15% v/v or 10% w/w.	1 to 4 dr. (4 to 16 mils).
Malti cum Oleo Vitaminato	Incorporate Vitamised oil with Extract of Malt.	15% v/v or 10% w/w.	1 to 4 dr. (4 to 16 mils). 4 dr. = approx. 2500 units Vit. A: 8250 ,, Vit. B.

DRY EXTRACTS

EXTRACTUM.	METHOD.	STRENGTH.	DOSE.
Belladonnæ Siccum	Percolate dried leaf with 70% alcohol. Assay for total solids and total alkaloids. Add a calculated quantity of standardized powdered leaf and evaporate to dryness.	1% total alkaloids.	¼ to 1 gr. (0·015 to 0·06 gm.).
Cascara Sagradæ Siccum	Exhaust the bark by percolation with water. Evaporate the percolate to dryness under reduced pressure.		2 to 8 gr. (0·12 to 0·5 gm.).
Colchici Siccum	Exhaust dried corm by percolation with 60% alcohol. Evaporate to a thin syrupy liquid, assay, add calculated amount of lactose and evaporate to dryness.	1% colchicine.	¼ to 1 gr. (0·015 to 0·06 gm.).
Coloc. Comp.	Extract the Colocynth pulp by maceration with 60% alcohol. Evaporate the macerate to dryness; add Aloe, Scammony Resin, Cardamom, and Curd Soap.		2 to 8 gr. (0·12 to 0·5 gm.).
Hepatis Siccum	An alcoholic extract of fresh ox liver.		The equivalent of ½ lb. fresh liver.
Hyoscyami Siccum	Percolate dried leaf with 70% alcohol. Assay for total solids and total alkaloids. Add the calculated quantity of standardized powdered leaf and evaporate to dryness.	0·3% total alkaloids.	¼ to 1 gr. (0·016 to 0·06 gm.).
Krameria Siccum	Exhaust the root by percolation with water. Evaporate to dryness under reduced pressure.		5 to 15 gr. (0·3 to 1 gm.).
Nucis Vomicæ Siccum	Exhaust the seeds by percolation with 70% alcohol. Evaporate off the alcohol. Defat with melted paraffin wax, assay, add the calculated amount of calcium phosphate and evaporate to dryness.	5% strychnine.	¼ to 1 gr. (0·015 to 0 06 gm.).
Opii Siccum	Exhaust opium with hot water. Assay for total solids and morphine. Add the calculated amount of calcium phosphate and evaporate to dryness.	20% morphine.	¼ to 1 gr. (0·015 to 0·06 gm.).
Stramonii Siccum	Percolate dried leaf with 95% alcohol. Assay for total solids and total alkaloids. Add a calculated quantity of starch, and evaporate to dryness.	1% total alkaloids.	¼ to 1 gr. (0·015 to ·006 gm.). Post encephalitic 1 to 8 gr. (0·06 to 0·5 gm.).

LIQUID EXTRACTS

EXTRACTUM.	METHOD.	STRENGTH.	DOSE.
Belladonnæ Liq.	Exhaust the root by percolation with 90% alcohol and water. Assay and adjust.	0·75% w/v total alkaloids.	¼ to 1 min. (0·015 to 0·06 mil).
Cascaræ Sagradæ Liq.	Exhaust the bark by percolation with water. Concentrate and add 90% alcohol.	1 in 1.	½ to 1 dr. (2 to 4 mils).
Cinchonæ Liq.	Exhaust the bark with mixture of water, hydrochloric acid and glycerin. Concentrate, assay, add 90% alcohol and adjust.	5% w/v total alkaloids.	5 to 15 min. (0·3 to 1 mil).
Colchici Liq.	Defat the seeds with petroleum spirit. Exhaust the defatted seeds with 60% alcohol. Assay and adjust.	0·3% w/v Colchicine.	2 to 5 min. (0·12 to 0·3 mil).
Ergotæ Liq.	Ergot extracted with acidified (Tartaric Acid) alcohol 50%.	0·06% Ergotoxine.	10 to 20 min. (0·6 to 1·2 mils).
* Filicis	Exhaust male fern rhizome with ether. Evaporate off the ether. Assay and adjust the strength with olive oil.	25% w/w Filicin.	45 to 90 min. (3 to 6 mils).
Hepatis Liq.	An alcoholic extract of fresh ox liver.		1 fl. oz. (30 mils).
Glycyrrhizæ Liq.	Exhaust the root with chloroform water, boil, filter, evaporate until S.G. 1·20. Add 90% alcohol.		½ to 1 dr. (2 to 4 mils).
Hamamelidis Liq.	Exhaust the dried leaf by percolation with 45% alcohol, reserve the first portion, evaporate the remainder to low bulk and dissolve in the first portion.	1 in 1.	½ to 1 dr. (2 to 4 mils).
Hyoscyami Liq.	Exhaust the dried leaf by percolation with 70% alcohol. Reserve the first portion, evaporate the remainder to low bulk, dissolve in the first portion, assay and adjust to volume.	0·05% w/v. Hyoscyamine.	3 to 6 mins. (0·2 to 0·4 mil).
Ipecacuanhæ Liq.	Exhaust the root by percolation with 90% alcohol. Reserve the first portion, evaporate the remainder to low bulk, dissolve in the first portion, assay and adjust to volume.	2% w/v total alkaloids.	½ to 2 min. or 10 to 30 min.
Nucis Vomicæ Liq.	Exhaust the seeds by percolation with 70% alcohol, concentrate to low bulk, defat with melted paraffin wax, add 70% alcohol, filter, assay, adjust to volume with 45% alcohol.	1·5% strychnine.	1 to 3 mins. (0·06 to 0·2 mil).

* Included because it is a thick liquid.

LIQUID EXTRACTS—*continued*

EXTRACTUM.	METHOD.	STRENGTH.	DOSE.
Pituitarii Liq.	Posterior lobes extracted with hot water acidulated with acetic acid, the solution sterilized and transferred to glass containers.		2 to 5 units (0·2 to 0·5 mil).
Senegæ Liq.	Exhaust Senega by percolation with 60% alcohol. Reserve the first portion, evaporate the remainder to low bulk, dissolve in the first portion, add solution of ammonia and adjust to volume with 60% alcohol.	1 in 1.	5 to 15 min. (0·3 to 1 mil).
Sennæ Liq. . .	Extract Senna Pods by a triple maceration with chloroform water. Concentrate under reduced pressure, add 90% alcohol, adjust to volume with water.	1 in 1.	10 to 30 min. (0·6 to 2 mils).
Stramonii Liquidum	Percolate with 45% alcohol. Reserve the first portion, evaporate the remainder to a soft extract and dissolve in the reserved portion. Assay and adjust.	0·25% total alkaloids.	½ to 3 min. (0·03 to 0·2 mil).

Glycerina.—Glycerins are solutions of medicaments in glycerin and are often used as throat paints. The high viscosity of the glycerin is useful in causing the preparation to adhere to the mucous surface for a longer period than would an aqueous solution. The demulcent action of the glycerin is often a useful adjunct to the action of the medicament. The student should particularly remember that whilst a solution of phenol in glycerin is not caustic, a solution in water may be very caustic, and therefore glycerin of phenol when required of a weaker strength should be diluted with glycerin and *not water*. Glycerin of starch is used as an ointment base.

GLYCERINS

GLYCERINUM.	STRENGTH.
Acidi Borici	31% w/w.
Acidi Tannici	15% ,,
Aluminis	13% ,,
Amyli	—
Boracis	12% ,,
Phenolis	16% ,,

Infusa (Infusions), see also p. 242.—These are aqueous solutions of vegetable principles. The Pharmacopœia provides two methods of preparation : (*a*) By infusing the drug

in a suitable state of comminution with (usually) boiling water for a definite time, and then straining. Two, Calumba and Quassia, are made with cold water. The Pharmacopœia directs that they shall be used within 12 hours of preparation. These infusions are known as "fresh" infusions, such as Inf. Buchu Recens, and prescribers should note that *if they wish these fresh infusions to be dispensed* they must specify "*Recens*" on the prescription. (*b*) By the dilution of the Concentrated Infusions. These are either weak alcoholic (25%) solutions of the drug principles or strong aqueous solutions containing some alcohol as a preservative. When these concentrated infusions are diluted 1 in 8 with distilled water they give a product which resembles to some extent the fresh infusions. These preparations may be dispensed if the prescriber does not specify *recens*.

NOTE.—Infusion of Digitalis is always to be made fresh, no concentrated preparation occurring in the Pharmacopœia. All the other fresh infusions have corresponding concentrated infusions.

INFUSA RECENTIA (FRESH INFUSIONS)

INFUSUM RECENS.	INGREDIENTS.	TIME.	DOSE.
Aurantii ..	Dried bitter-orange peel cut small and boiling water.	15 minutes.	½ to 1 fl. oz. (15 to 30 mils).
Buchu ..	Leaves freshly broken and boiling water.	15 minutes.	1 to 2 fl. oz. (30 to 60 mils).
Calumbæ ..	Root cut small and *cold* water.	30 minutes.	½ to 1 fl. oz. (15 to 30 mils).
Caryophylli ..	Clove bruised and boiling water.	15 minutes.	½ to 1 fl. oz. (15 to 30 mils).
Digitalis ..	Powdered Digitalis, boiling water.	15 minutes.	90 to 300 min.; single dose 1 to 4 fl. oz.
Gentianæ Co.	Root thinly sliced, dried bitter-orange peel, fresh lemon peel cut small and boiling water	15 minutes.	½ to 1 fl. oz. (15 to 30 mils).
Quassiæ ..	Wood rasped and *cold* water.	15 minutes.	½ to 1 fl. oz. (15 to 30 mils).
Senegæ ..	Root in coarse powder and boiling water.	30 minutes.	½ to 1 fl. oz. (15 to 30 mils).
Senna	Senna pods, sliced ginger and boiling water.	15 minutes.	½ to 2 fl. oz. (15 to 60 mils).

Injectiones (Injections) (also p. 218 et seq.).—The Pharmacopœia describes 6 injections, 5 of which are intramuscular injections, and one (Inj. Sod. Chlor. et Acac.) is for intravenous use. Liquor Sodii Chlorid: Physiologicus is often used for intravenous injection ("Normal") saline. The various addenda have added to the number of injections. All are summarized in the following table.

The new Addenda to the Pharmacopœia has added 6 more injections. All these are included below.

INJECTIONS

INJECTION.	COMPOSITION.	STRENGTH.	DOSE.
Inj. Bismuthi	Precipitated Bismuth metal, finely divided and suspended in a solution of dextrose and cresol.	20% w/v Bi.	8 to 15 min. (0·5 to 1 mil).
Inj. Bismuthi Salicyl.	Bismuth Salicylate, finely suspended in olive oil solution of camphor and phenol.	10% w/v Bism. Salicyl.	10 to 20 min. (0·6 to 1·2 mil).
Inj. Bismuthi Oxychloridi	Bismuth Oxychloride, suspended in a solution of dextrose and cresol.	30 min. contain about 3 gr. Bism. Oxychloride.	15 to 30 min. (1 to 2 mils) intramuscular.
Inj. Calcii Gluconatis	Solution in water.	300 min. contain about 30 grain Calc. Gluconate.	150 to 300 min. (10 to 20 mils).
Inj. Ferri	Freshly prepared ferric hydroxide dissolved in citric acid, and neutralized with dilute ammonia.	30 min. contain equivalent of ½ gr. of Ferri Ammon. Cit.	15 to 30 min. (1 to 2 mils) intramuscular.
Inj. Hydrarg.	Mercury finely suspended in olive oil solution of camphor and creosote.	10% w/w Hg.	5 to 10 min. (0·3 to 0·6 mil) intramuscular.
Inj. Hydrarg. Subchlor.	Calomel finely suspended in olive oil solution of camphor and creosote.	5% w/w Hg_2Cl_2	10 to 20 min. (0·6 to 1·2 mils) intramuscular.
Inj. Leptazol.	Leptazol, dissolved in water; adjusted to *p*H 7·8.	10 w/v Leptazol.	8 to 15 min. (0·5 to 1·0 mil) subcutaneous 30 to 75 increasing to 180 min (2 to 5 mils, increasing to 12 mils) as convulsant.
Inj. Mersalyli	A solution of Mersalyl and Theobromine in water; adjusted to *p*H 7·8, with Sodium Hydroxide	10% w/v Mersalyl.	8 to 30 min. (0·5 to 2·0 mils).
Inj. Nikethamidi.	Solution in water.	25% w/v Nikethamide	15 to 60 min. (1 to 4·0 mils) subcut. or intramuscular. 75 to 240 min. (5 to 16 mils) intravenous as convulsant.
Inj. Procain. et Adrenalin.	Solution of both in water, with chlorcresol, and sodium metabisulphite.	2% Procaine ·002% Adrenaline.	—
Inj. Quin. et Urethan.	Solution in water with Chlorcresol.	12·5% Quin. Hyd. 6·25% Urethane.	8 to 75 min. (0·5 to 5 mils) intravenous as sclerosing agent.

INJECTION.	COMPOSITION.	STRENGTH.	DOSE.
Inj. Sod. Chlor. et Acaciæ.	Solution in water.	6·0% Acacia. 0·9% NaCl.	—
Inj. Sod. Morrhuat.	Solution in water, with chlorcresol and 1% alcohol.	5% Sod. Morrhuat.	8 to 75 min. (0·5 to 5·0 mils) intravenous as sclerosing agent.

Lamellæ (Discs) are 4 in number. They are for introduction into the eye : .

Lamellæ Atropinæ—Discs of gelatin and some glycerin, each weighing about $\frac{1}{50}$ gr., and containing $\frac{1}{5000}$ gr. atropine sulphate.

Lamellæ Cocainæ—Discs of gelatin, with some glycerin, each weighing about $\frac{1}{20}$ gr., and containing $\frac{1}{50}$ gr. cocaine hydrochloride.

Lamellæ Homatropinæ—Discs of gelatin, with some glycerin, each weighing about $\frac{1}{50}$ gr., and containing $\frac{1}{100}$ gr. of homatropine hydrobromide.

Lamellæ Physostigminæ—Discs of gelatin, with some glycerin, each weighing about $\frac{1}{50}$ gr., and containing $\frac{1}{1000}$ gr. physostigmine salicylate.

They are made by pouring a warm solution of the drug in water, glycerin and gelatin on to a sheet of glass ; after drying, circular discs are cut out with a diameter of 3·17 millimetres.

Linimenta (Liniments).—These are preparations for external application to the skin and intended to be applied with friction. When alcohol is an ingredient, it may be replaced with industrial methylated spirit of equivalent strength.

LINIMENTS

LINIMENTUM.	COMPOSITION.	STRENGTH.
Aconiti.. ..	Root, camphor (3%), and alcohol (90%).	1 in 2. Root.
Belladonnæ ..	Root extracted with alcohol (90%), also containing camphor, assayed and adjusted to strength.	0·375% alkaloids.
Camphoræ ..	Camphor (in flowers) 1, and olive oil 4.	20%.
Camphoræ Ammoniatum	Camphor, oil of lavender, strong solution of ammonia, and alcohol (90%).	12½%.
Saponis ..	Soft soap, camphor, oil of rosemary, distilled water, and alcohol (90%).	8%.
Terebinthinæ..	Soft soap, camphor, oil of turpentine and water.	65%.
Terebinth. Acet... ..	Glacial acetic acid, camphor liniment, oil of turpentine.	44%.

Liquores (Liquors).—These are generally aqueous solutions of potent drugs often containing some alcohol as a preservative. The following are all 1 per cent. w/v or 1 gr. in 110 min.:

Arsenicalis, Arseni et Hydrarg. Iodid., Glyceryl. Trinitrat., Morph. Hydrochlor., Strychnin. Hydrochlor.

LIQUORS OR SOLUTIONS

LIQUOR.	STRENGTH.	DOSE.
Adrenalini Hydrochloricus ..	1 in 1000, or 0·1%.	2 to 8 min.
Ammoniæ Dilutus	10% w/w.	Used externally.
Ammoniæ Fortis	32·5% w/w.	Used externally.
Ammonii Acetatis Dil. ..	about 7·2%.	½ to 1 fl. oz.
Ammonii Acetatis Fort. ..	57½%.	15 to 60 m.
Arsenicalis	1%; 1 gr. in 110 min.	2 to 8 m.
Arseni et Hydrg. Iod. ..	1%; 1 gr. in 110 min.	5 to 15 m.
Liquor Calciferolis	3000 units of antirachitic activity in 1 gm.	5 to 10 min. (infant, daily) (prophylactic) 10 to 15 min. (infant, daily) (therapeutic).
Calcii Hydroxidi	1%; $\frac{1}{10}$ gr. in 110 min.	1 to 4 oz.
Cresolis Saponatus	50%	Used externally.
Epispasticus	0·4%.	Used externally.
Ferri Perchloridi	15%.	5 to 15 m.
Formaldehydi	37 to 41%.	Used externally.
Glycerylis Trinitratis ..	1%.	½ to 2 m.
Hydrargyri Perchloridi ..	0·1%; $\frac{1}{10}$ gr. in 110 min.	½ to 1 dr.
Hydrogenii Peroxidi	10 of oxygen in 1.	½ to 2 dr.
Liquor Iodi Aquosus ..	5% iodine. 10% potassium iodide	5 to 15 min.
Iodi Fortis	10%.	Used externally.
Iodi Mitis	2½%.	5 to 30 m.
Iodi Simplex	9%.	3 to 15 m.
Magnesii Bicarbonatis ..	2½%.	1 to 2 oz.
Morphinæ Hydrochloridi ..	1%; 1 gr. in 110 min.	5 to 30 m.
Picis Carbonis	20%.	Used externally.
Plumbi Subacetatis Fortis ..	25%.	Used externally.
,, ,, Dilutus	12½% of liquor.	Used externally.
Potassii Hydroxidi	5%; 5 gr. in 110 min.	Used externally.
Quininæ Ammoniatus ..	2%.	½ to 1 dr.
Sodæ Chlorinatæ Chirurg. ..	0·5% Cl.	Used externally.
Sod. Chlor. Physiolog. ..	0·9%.	—
Sodii Hydroxidi	3·56% NaOH	—
Strychninæ Hydrochloridi ..	1%; 1 gr. in 110 min.	3 to 12 m.
Vitamini A Conc.	50,000 units per gramme.	1 to 5 min.
Vitamini A et D Conc. ..	50,000 units A 5,000 units D per gramme.	—
Vitamini D conc.	10,000 units per gramme.	½ to 3 min.

Lotiones (Lotions) are liquid preparations for external application. Only one is official:

Lotio Hydrargyri Nigra—Calomel, glycerin, and lime water (black wash).

Mella (Honeys—4 in number) are preparations of honey:

Mel Depuratum—Honey melted and strained through flannel; S.G. adjusted to 1·36 by water if necessary.

Mel Boracis—Purified borax, mixed with purified honey and glycerin.

Oxymel—Acetic acid, purified honey, and distilled water. *Dose*—1 to 2 dr.

Oxymel Scillæ—Squill, acetic acid water, purified honey. *Dose*—½ to 1 dr.

Misturæ (Mixtures, 2 in number).—These represent two well-known purgative preparations:

Mist. Magnesii Hydroxidi—A suspension of freshly precipitated magnesium hydroxide and light magnesium oxide in water. *Dose*—1 to 4 dr.

Mist. Sennæ Co.—Magnesium sulphate, liquid extract of liquorice, compound tincture of cardamom, aromatic spirit of ammonia, fresh infusion of senna. *Dose*—1 to 2 fl. ozs.

Mucilagines (Mucilages).—These are aqueous solutions of gums:

Mucilago Acaciæ—Acacia 40, dissolved in chloroform water 60. *Dose*—1 to 4 dr.

Mucilago Tragacanthæ—Tragacanth 12½, alcohol 25, chloroform water to 1000. *Dose*—1 to 4 dr.

Oculenta (Ointments for the Eye).—The Pharmacopœia describes a general process to be followed in making ointments for the eye. The base is prepared by melting together soft paraffin and wool fat, filtering the melted mixture through coarse filter-paper and sterilizing in a hot-air oven at 150° for one hour. This sterilized base should be used for the preparation, under aseptic conditions, of all eye ointments.

When the drug is the salt of an alkaloid, the quantity

required is placed in a sterilized mortar and dissolved in the minimum amount of water. This solution is then incorporated in the melted base by trituration. Any other drug is incorporated directly in the melted base after being finely powdered and levigated down with a little of the base.

Ointments for the Eye are best dispensed in collapsible tubes.

If the prescriber does not specify the strength, the following should be supplied:

OCULENTUM.	INGREDIENTS.	STRENGTH.
Atropinæ	Atropine sulphate.	0·25%.
Atropinæ cum Hydrarg. Oxid.	Atropine sulphate. Yellow mercuric oxide.	0·125%. 1%.
Cocainæ	Cocain. hydrochlor.	0·25%.
Hydrarg. Oxidi	Yellow mercuric oxide.	1%.
Hyoscinæ	Hyoscin. hydrobrom.	0·125%.
Iodoformi	Iodoform.	4%.
Physostigminæ	Physostigmin. salicyl.	0·125%.

Olea (Oils).—Oils may be divided into two classes—fixed and volatile.

Fixed Oils are those which cannot be distilled without decomposing, and are, therefore, obtained by hot or cold expression, or by the use of solvents. They can be divided into two classes—fats and waxes. *Fats* are those fixed oils which consist mainly of the glyceryl esters of fatty acids and which, on hydrolysis, produce glycerin. All the fixed oils called oils in the Pharmacopœia are of this type, and in addition such substances as lard and suet come under this classification. On keeping they tend to go rancid, developing a disagreeable odour and free acid. In this condition they may be irritating when applied to tender surfaces, particularly when used as a basis for preparations intended for application to the eye. Reasonable care should be taken in the storage of them—cod-liver oil, particularly, should be stored in well-filled, well-closed containers and protected from the light. *Waxes* are those fixed oils which have any other base than glycerin. There are no liquid waxes in the Pharmacopœia, but solid ones such as beeswax and wool fat occur.

Volatile Oils are aromatic compounds which can be obtained by distillation without decomposition. The minimum amount of heat must be used if the full odour is to be pre-

served, and it is usual to employ steam distillation in their preparation. One volatile oil—oil of lemon—is, however, expressed. Oil of cade is a volatile oil obtained by the dry heating of the wood of *Juniperus oxycedrus*. Decomposition occurs with the production of volatile decomposition products which distil over and are condensed. This process is known as distinctive distillation. Pix liquida (Stockholm Tar) and Pix carbonis (Coal Tar) are also products of the destructive distillation of pinewood and coal respectively.

In the English names of oils, as a convention, the specific name precedes the word "oil" in the case of fixed oils—e.g. almond oil—and follows it in the case of the volatile oils—e.g. oil of peppermint.

VOLATILE OILS

OLEUM.	SOURCE AND HOW PREPARED.	DOSE.
Abietis ..	Distilled from fresh leaves of *Abies sibirica.*	—
Amygdalae Volatile, Purification	Distilled from almonds, peach kernels, apricot kernels, after removal of fixed oil. HCN removed.	½ to 1 min.
Anethi ..	Distilled from dill fruit.	1 to 3 min.
Anisi	Distilled from the fruit of anise or star-anise.	1 to 3 min.
Cadinum ..	Obtained by the *destructive* distillation of the wood of *Juniperus Oxycedrus.*	Used externally.
Cajuputi ..	Distilled from the leaves of *Melaleuca Leucadendron* and other species.	1 to 3 min.
Cari	Distilled from caraway fruit.	1 to 3 min.
Caryophylli ..	Distilled from the flower buds.	1 to 3 min.
Chenopodii ..	Distilled from the plant.	3 to 15 min.
Cinnamomi ..	Distilled from cinnamon bark.	1 to 3 min.
Coriandri ..	Distilled from the fruit.	1 to 3 min.
Eucalypti ..	Distilled from the fresh leaves.	1 to 3 min.
Hydnocarpi Æthyl.	Ethyl esters of fatty acids of hydnocarpus oil.	5 to 15 min., increasing to 60 min.
Lavandulæ ..	Distilled from the flowers.	1 to 3 min.
Limonis ..	Expressed from the fresh peel.	1 to 3 min.
Menthæ Piperitæ	Distilled from the fresh flowering *M. piperita.*	1 to 3 min.
Myristicæ ..	Distilled from the dried kernels.	1 to 3 min.
Rosmarini ..	Distilled from the flowering tops of *R. officinalis.*	1 to 3 min.
Santali ..	Distilled from the wood of *Santalum album.*	5 to 15 min.
Santali Australiensis	Distilled from the wood of *Eucarya spicata.*	5 to 15 min.
Terebinthinæ	Distilled from the oleo-resin of various pines, and rectified.	2 to 10 min. 2 to 4 dr. as anthelmintic.

FIXED OILS

OLEUM.	SOURCE AND HOW PREPARED.	DOSE.
Amygdalæ ..	Expressed from bitter and sweet almonds.	½ to 1 fl. oz.
Arachis ..	Expressed from seeds.	½ to 1 fl. oz.
Gossypii Seminis	,, ,, ,,	½ to 1 fl. oz.
Hippoglossi ..	Expressed fresh halibut livers.	1 to 5 min.
Hydnocarpi ..	Expressed from seeds	5 to 15 min., increasing to 60 min.
Lini	,, ,, ,,	½ to 1 fl. oz.
Morrhuæ ..	Expressed from fresh livers.	½ to 2 dr.
Olivæ	Expressed from ripe fruit.	½ to 1 fl. oz.
Ricini ..	Expressed from seeds.	1 to 4 dr.
Sesami ..	,, ,, ,,	½ to 1 fl. oz.
Theobromatis	,, ,, ,,	—
Vitaminatum	Solution of A and D in fish liver oil, or arachis oil.	15 to 30 min. (Prophylactic). 45 to 90 min. (Therapeutic).

Pilulæ (Pills) :—See also p. 193.

PILULA.	INGREDIENTS.	STRENGTH.
Aloes	Aloe, hard soap, oil of caraway, syrup of liquid glucose.	58% aloe.
Aloes et Asafetidæ ..	Aloe, asafetida, hard soap, syrup of liquid glucose.	30%.
Aloes et Ferri ..	Exsiccated ferrous sulphate, aloe, cinnamon, cardamom, ginger, syrup of liquid glucose.	20% aloe. 10% Ferri Sulph. Exsic.
Colocynthidis et Hyoscyami	Colocynth, aloe, scammony resin, hard soap, oil of clove, dry extract of hyoscyamus, syrup of liquid glucose.	12·5% of each.
Ferri Carbonatis ..	Exsiccated ferrous sulphate, exsiccated sodium carbonate, tragacanth, acacia, liquid glucose, distilled water.	20% carbonate.
Hydrargyri	Mercury, syrup, liquid glucose, glycerin, liquorice in powder.	33%.
Rhei Comp.	Rhubarb, aloe, myrrh, hard soap, oil of peppermint, syrup of liquid glucose.	25%.

They are soft masses, capable of being easily moulded into pill form. The dose of one, Pil. Ferri Carb., is 5 to 15 gr., whilst that of all the others is 4 to 8 gr.

Pulveres (Powders) :—See also p. 178.

PULVIS.	INGREDIENTS.	DOSE.	STRENGTH.
Cretæ Aromaticus	Chalk, cinnamon, nutmeg, clove, cardamom, sucrose.	10 to 60 gr. (0·6 to 4 gm.).	50% chalk.
Cretæ Aromaticus cum Opio	Aromatic powder of chalk, opium.	10 to 60 gr. (0·6 to 4 gm.).	2·5% opium.
Effervescens Comp.	In blue paper: sodium potassium tartrate, 7·5 gm.; sodium bicarbonate 2·5 gm. In white paper: tartaric acid, 2·5 gm.	One of each mixed in water.	—
Glycyrrhizæ Comp.	Senna leaves, peeled liquorice, fennel, sublimed sulphur, sucrose.	1 to 2 dr. (4 to 8 gm.).	16% of senna.
Ipecacuanhæ et Opii	Ipecacuanha, opium, lactose.	5 to 10 gr. (0·3 to 0·6 gm.).	10% opium and ipecacuanha.
Jalapæ Comp. ..	Jalap, potassium acid tartrate, ginger.	10 to 60 gr. (0·6 to 4 gm.).	30% jalap.
Rhei Comp. ..	Rhubarb, heavy and light magnesium, carbonate ginger.	10 to 60 gr. (0·6 to 4 gm.).	25% rhubarb.
Tragacanthæ Comp.	Tragacanth, acacia, starch, sucrose.	10 to 60 gr. (0·6 to 4 gm.).	—
Vitamin B_1 ..	An adsorbate of Vitamin B_1 on Fuller's earth.	15 to 30 gr. (prophylactic, daily) 30 to 90 gr. (therapeutic, daily)	100 units of antineuritic activity per gramme.

The student should learn to distinguish these compound powders by appearance and odour. The opium in pulv. cret. aromat. cum opio will distinguish it from pulv. cret. aromat. alone.

Sera. (See under Antitoxins, p. 275.)

Spiritus (Spirits).—These are, for the most part, alcoholic solutions of a volatile oil and often known as "Essences." Such spirits, if cloudy when prepared, are clarified by shaking with talc and filtering.

SPIRITS

SPIRITUS.	COMPOSITION.	STRENGTH.	DOSE.	SYNONYMS.
Ætheris ..	Ether 1, alcohol (90%) 2.	33%.	15 to 60 m. (1 to 4 mils).	—
Ætheris Nitrosi	An alcoholic solution containing ethyl nitrite, traces of acetaldehyde and other related substances.	1·25 to 2·5% w/v ethyl nitrite.	15 to 60 m. (1 to 4 mils).	Sweet spirit of nitre.
Ammoniæ Aromaticus	Ammonium carbonate, strong solution of ammonia, oil of nutmeg, oil of lemon, alcohol (90%) and water.	2·1 to 2·4% w/v NH_3.	15 to 60 m. (1 to 4 mils).	Sal volatile.
Cajuputi ..	Oil of cajuput and alcohol (90%).	10%.	5 to 30 m. (0·3 to 2 mils).	—
Camphoræ	Camphor and alcohol (90%).	10%.	5 to 30 m. (0·3 to 2 mils).	—
Chloroformi	Chloroform and alcohol (90%).	5%.	5 to 30 m. (0·3 to 2 mils).	Chloric ether. Spirits of chloric ether.
Menthæ Piperitæ	Oil of peppermint and alcohol (90%).	10%.	5 to 30 m. (0·3 to 2 mils).	Essence of peppermint.
Methylatus Industrialis	Alcohol (95%) 19; wood naphtha 1.	—	—	Industrial methylated spirits.

Suppositoria (Suppositories) (also p. 201).—Suppositories are directed to be made with a basis of oil of theobroma unless otherwise directed; the melting-point may be raised, if necessary, to 37°, but not higher, by the addition of white beeswax. This is sometimes necessary with certain medicaments such as phenol, which tends to lower the melting-point of oil of theobroma when melted with it.

In the case of the following suppositories, if the doses of the drugs are not stated by the prescriber, suppositories containing the following quantities shall be dispensed:

SUPPOSITORIA.	STRENGTH.
Acidi Tannici	3 gr. (0·2 gm.).
Belladonnæ	2½ min. (0·15 mil) liquid extract.
Iodoformi	3 gr. (0·2 gm.).
Morphinæ	¼ gr. (0·015 gm.) morph. hydrochloride.
Phenolis	1 gr. (0·06 gm.).
Plumbi cum Opio ..	Lead acetate 3 gr. (0·2 gm.). Opium 1 gr. (0·06 gm.).

A special formula is laid down for glycerin suppositories as follows: Gelatin 14, glycerin 70, water to 100. Glycerin suppositories are prescribed in three sizes: Infants (15 gr. mould), children (30 gr. mould), and adults (60 gr. mould).

Syrupi (Syrups)—are strong solutions of sucrose containing medicaments or flavouring agents. The sucrose is of value because of its demulcent properties and its sweetness, as well as its preservative action on vegetable principles. If the concentration of sucrose is less than that in simple syrup, the syrup may ferment on keeping unless some preservative is present to prevent it. The dose of all the syrups is ½ to 2 drs., except those of Easton's Syrup and Syrup of Squills, which are ½ to 1 dr.

SYRUPS

SYRUPUS.	INGREDIENTS.	STRENGTH.	DOSE.
Syrupus	Sucrose and water.	1 in 1½ w/w.	—
Aurantii	Tincture of orange 12½, and syrup to 100.	12½% v/v.	½ to 2 dr. (2 to 8 mils).
Ferri Iodidi ..	Iron, iodine, dilute hypophosphorous acid, water and syrup.	5% w/w ferrous iodide.	½ to 2 dr. (2 to 8 mils).
Ferri Phosphatus Comp. (Parrish's Food)	Iron, phosphoric acid, calcium carbonate, potassium bicarbonate, sodium phosphate, cochineal, sucrose, triple orange flower water and water.	0·9% w/v iron.	½ to 2 dr. (2 to 8 mils).
Ferri Phosphatis cum Quinina et Strychnina (Easton's Syrup)	Iron, phosphoric acid, strychnine hydrochloride, quinine sulphate, syrup, glycerin and water.	1 dr. contains strychnine $\frac{1}{64}$ gr., quinine $\frac{4}{5}$ gr.	½ to 1 dr. (2 to 4 mils).
Glucosi Liquidi ..	Liquid glucose 1, and syrup 2.	33%.	—
Limonis	Lemon peel, alcohol, citric acid and syrup.	—	½ to 2 dr.
Pruni Serotinæ (Virginian Prune)	Wild cherry bark, sucrose, glycerin and water.	15%.	½ to 2 dr.
Scillæ	Vinegar of squill, sucrose and water.	4·5% squill.	½ to 1 dr.
Sennæ	Liquid extract of senna, oil of coriander, sucrose and water.	25% liquid extract.	½ to 2 dr.
Tolutanæ	Balsam of tolu, sucrose and water.	2·5%.	½ to 2 dr.
Zingiberis ..	Strong tincture of ginger and syrup.	5% strong tincture.	½ to 2 dr.

Tabellæ (Tablets).—Only one preparation is official:

Tabella Glycerylis Trinitratis (Synonyms—Tabellæ Trinitrini; Tablets of Nitroglycerin)—Tablets with a

chocolate base each weighing 0·3 gm. and containing 0·0005 gm. ($\frac{1}{120}$ gr.) glyceryl trinitrate $C_3H_5(NO_3)_3$. *Dose*—1 to 2 tablets.

Tincturæ (Tinctures).—Tinctures are alcoholic solutions of the active principles of drugs, and are prepared by the following processes (see also pp. 242, 243):

(*a*) *Maceration.*—The solid materials are placed with the whole of the menstruum in a closed vessel, and shaken occasionally during 7 days. It is then strained, the marc pressed, the expressed liquid added to the strained liquid, and the whole clarified by subsidence or filtration. It is not made up to volume.

(*b*) *Maceration with Adjustment to Volume.*—The drugs extracted by the previous maceration process leave a fair amount of fibrous residue after extraction which can be readily pressed. When, however, drugs which are of a resinous or gummy nature, such as oleo gum resins (e.g. Myrrh), are to be extracted, the gummy residue cannot be pressed. It is, therefore, washed with more menstruum, the washings added to the strained portion, and the whole adjusted to a definite volume. In this respect it differs from the ordinary *maceration* process.

(*c*) *Percolation.*—The solid materials are moistened with a certain amount of the menstruum and set aside for 4 hours in a well-closed vessel. This permits the drug to swell and the solvent to penetrate the tissues. It is then packed in a percolator and sufficient menstruum added to saturate it, and when the liquid commences to drip from the percolator, the outlet is closed and menstruum added until a layer is left above the drug. It is macerated for 24 hours, and then percolation is allowed to proceed slowly until the percolate measures about $\frac{3}{4}$ of the volume required for the finished tincture. The marc or residue is then pressed, the expressed liquid mixed with the percolate, and sufficient menstruum added to produce the required volume. It is then clarified by subsidence or filtration.

(*d*) *Simple Solution.*—Some tinctures are made by dilution of a liquid extract or stronger tincture with the same menstruum used in the preparation of the latter preparations. Certain preparations, formerly known as tinctures and prepared by the simple solution of chemical substances, are now known as liquors. These are: Liquor Iodi Mitis

(Synonym—Tincture of Iodine); Liquor Iodi Fortis (Synonym—Strong Tincture of Iodine); Liquor Quininæ Ammoniatus (Synonym—Ammoniated Tincture of Quinine).

Strengths.—The strength of most of the tinctures depends upon the amount of crude drug employed, but the more important ones are standardized either—(*a*) so that they contain a definite amount of active principle (these are usually tinctures made from alkaloidal or resinous drugs and the method of assay is a chemical one); or (*b*) so that they have a definite potency towards certain animals under specified conditions. This method of standardization is known as a biological method.

The following tinctures are standardized:

Chemical Assay—Belladonna, Cinchona, Cinchona Co., Colchicum, Hyoscyamus, Ipecacuanha, Nux Vomica, Opium, Tinct. Opii Camph., Stramonium.

Biological Assay—Digitalis, Strophanthus.

Dosage.—The dose of the majority of tinctures is ½ to 1 dr. The others are as follows:

30 to 90 minims—Digitalis (single dose).
10 to 30 minims—Ipecacuanha, Nux Vomica.
5 to 30 minims—Belladonna, Opium, Squill, Stramonium.
5 to 15 minims—Capsicum, Cochineal, Colchicum, Digitalis (repeated dose), Lobelia.
5 to 10 minims—Ginger (Strong tincture).
2 to 5 minims—Strophanthus.

Tincture of Ipecacuanha has an emetic dose ½ to 1 fl. oz.

The method of preparation is indicated in the table on this and the following page.

M = Maceration.
MM = Maceration with adjustment to volume.
P = Percolation.
S = Simple solution.

TINCTURES

TINCTURA.	INGREDIENTS.	STRENGTH.	METHOD.	DOSE.
Asafetidæ ..	Asafetida, alcohol (70%).	20%.	MM.	½ to 1 dr.
Aurantii ..	Fresh bitter peel, alc.(90%).	25%.	M.	½ to 1 dr.
Belladonnæ..	Leaf, alc. (70%).	0·03% alkaloids.	P.	5 to 15 min.
Benzoin Co.	Benzoin, storax, tolu, aloes, alc. (90%).	10%.	MM.	½ to 1 dr.
Calumbæ ..	Root, alc. (60%).	10%.	M.	½ to 1 dr.
Capsici ..	Fruits, alc. (60%).	5%.	M.	5 to 15 min.

TINCTURES—*continued*

TINCTURA.	INGREDIENTS.	STRENGTH.	METHOD.	DOSE.
Cardamom Co.	Cardamom, caraway, cinnamon, cochineal, glycerin, alc. (60%).	—	P.	½ to 1 dr.
Catechu ..	Catechu, cinnamon, alc. (45%).	20%.	M.	½ to 1 dr.
Cinchonæ ..	Extract, alc. (70%).	1% alkaloids.	S.	½ to 1 dr.
Cinchonæ Co.	Extract, dried bitter orange peel, serpentary, cochineal, alc. (70%).	0·5% alkaloids.	MM.	½ to 1 dr.
Cocci.. ..	Cochineal, alc. (45%).	10%.	M.	5 to 15 min.
Colchici ..	Liquid extract, alc. (60%).	0·03% Colchicine.	S.	5 to 15 min.
*Digitalis ..	Leaf, alc. (70%).	1 mil = 1 unit.	P. or M.	5 to 15 min. repeated 30 to 90 min.
Gentian Co.	Gentian, dried bitter orange peel, cardamom, alc. (45%).	10%.	M.	½ to 1 dr.
Hyoscyami ..	Liquid extract, alc. (70%).	0·005% Hyoscyamine.	S.	½ to 1 dr.
Ipecac. ..	Liquid extract, alc., water, glycerin.	0·1% Emetine.	S.	10 to 30 min. ½ to 1 fl. oz. (emetic).
Krameriæ ..	Root, alc. (70%).	20%.	P.	½ to 1 dr.
Limonis ..	Peel, alc. (60%).	25%.	M.	½ to 1 dr.
Lobel. Æther.	Lobelia, spirit of ether.	20%.	P.	5 to 15 min.
Myrrhæ ..	Myrrh, alc. (90%).	20%.	MM.	½ to 1 dr.
Nucis Vomicæ	Liquid extract, alc. (90%), water.	0·125% Strychnine.	S.	10 to 30 min.
Opii	Opium, alc. (90%), water.	1% Morphine.	MM.	5 to 30 min.
Opii Camph.	Tincture, benzoic acid, camphor, oil of anise, alc. (60%).	0·05% Morphine.	S.	½ to 1 dr.
Quassiæ ..	Quassia, alc. (45%).	10%.	M.	½ to 1 dr.
Quillaiæ ..	Quillaia, alc. (45%).	5%.	P.	½ to 1 dr.
Rhei Co. ..	Rhubarb, cardamom, coriander, glycerin, alc. (60%).	10%.	P.	½ to 1 dr.
Scillæ ..	Squill, alc. (60%).	10%.	M.	5 to 30 min.
Senegæ ..	Liquid extract, alc. (60%).	20%.	S.	½ to 1 dr.
Stramonii ..	Liquid extract, alc. (45%).	0·025% alkaloids.	S.	5 to 30 min.
Strophanthi	Seeds, alc. (70%).	International Standard.	P.	2 to 5 min.
Tolu	Tolu, alc. (90%).	10%.	MM.	½ to 1 dr.
Valerian Ammon.	Valerian, oils of nutmeg and lemon, dil. solution of ammonia, alc. (60%).	20%.	M.	½ to 1 dr.
Zingib. Fort.	Rhizome, alc. (90%).	50%.	P.	5 to 10 min.
Zingib. Mitis	Strong tincture, alc. (90%).	20%.	S.	½ to 1 dr.

* Two methods are permitted for the preparation of Tincture of Digitalis (see p. 368).

Toxinum Diphthericum Calefactum—Schick Control.—Schick Control is Toxinum Diphthericum Diagnosticum (Schick Test Toxin) which has been heated to a temperature of not less than 70° for not less than 5 minutes. *Dose*—By intradermal injection, 3 min. (0·2 mil).

Toxinum Diphthericum Detoxicatum—Diphtheria Prophylactic (also p. 148).—A sterile filtrate from a culture on nutrient broth of *Corynebacterium diphtheriæ*, the toxicity is reduced without lowering the antigenic value. *Dose*—By subcutaneous injection, the volume indicated on the label as the dose, on two or three occasions, at intervals of two to four weeks.

Toxinum Diphthericum Diagnosticum—Schick Test Toxin.—Schick Test Toxin is a reagent used for the diagnosis of susceptibility to diphtheria. It is prepared from a culture on nutrient broth of Corynebacterium diphtheriæ. *Dose*—By intradermal injection, 3 mins. (0·2 mil).

Toxinum Tetanicum Detoxicatum.—Tetanus Toxoid,—A sterile filtrate from a culture of *Clostridium tetani*, toxicity completely removed by chemical means, in such a manner that antigenic value retained. *Dose*—By subcutaneous or intramuscular injection, 15 mins (1·0 mil).

Trochisci (Lozenges).—These are small tablets composed of a sweet hard basis containing a medicament and intended to be slowly dissolved in the mouth. The majority are prepared with a general basis, whilst two, bismuth comp. and phenol, have special bases. The general basis is prepared from sucrose, acacia, tincture of tolu, and water.

LOZENGES

TROCHISCUS.	INGREDIENTS.	STRENGTH.
Acidi Tannici ..	Tannic acid, general basis.	½ gr.
Bismuthi Comp.	Bismuth carbonate, heavy magnesium carbonate, calcium carbonate, sucrose, acacia, oil of rose.	2½ gr. Bismuth Carbonate.
Krameriæ	Dry extract of krameria, general basis.	1 gr.
Krameriæ et Cocainæ	Dry extract of krameria, cocaine hydrochloride, general basis.	$\frac{1}{20}$ gr. Cocaine Hydrochloride.
Morphinæ et Ipecacuanhæ	Ipecacuanha, morphine hydrochloride, general basis.	$\frac{1}{72}$ gr. Morphine Hydrochloride, $\frac{1}{10}$ gr. Ipecacuanha.
Phenolis	Liquefied phenol, sucrose, acacia, tragacanth, citric acid, carmine.	½ gr. Phenol.

Tuberculinum Pristinum (Old Tuberculin).—Old Tuberculin is the concentrated filtrate from a fluid medium on which *Mycobacterium tuberculosis* has been grown. *Dose*—By subcutaneous injection: diagnostic, $\frac{1}{60}$ to $\frac{1}{12}$ min. (0·001 to 0·005 mil); therapeutic, $\frac{1}{60000}$ min. (0·000001 mil) gradually increased.

Note.—When Old Tuberculin is prescribed with the suffix T, the Old Tuberculin dispensed is prepared by growing the human type of bacilli. When prescribed with the suffix PT, the Old Tuberculin dispensed is prepared by growing the bovine type of bacilli.

Unguenta (Ointments) (see also p. 189).—The official ointments have 3 main bases—benzoinated lard, simple ointment, and paraffin ointment. All these bases keep well and do not go rancid. The lard basis is intended for those medicaments which are to be absorbed through the skin, such as belladonna and mercury. Simple ointment contains 5 per cent. wool fat, which permits it to take up appreciable quantities of aqueous liquids which neither of the other two bases will do.

When employing simple ointment or paraffin ointment as bases, white soft paraffin should be used for a white ointment and yellow soft paraffin for a coloured one.

In tropical and subtropical parts of the Empire more or less benzoinated lard, suet, yellow or white beeswax or lard may be employed in the preparation of the ointments when prevailing high temperatures render the basis too soft.

In India suet should be substituted for lard.

The following preparations, although not called ointments, are applied in a similar manner:

Gelatinum Zinci (Gelatin of Zinc; Unna's Paste)—Zinc oxide (15%), gelatin, glycerin, water.

Pasta Zinci Oxidi Composita (Compound Paste of Zinc Oxide; Zinc Paste)—Zinc oxide (25%), starch, soft paraffin.

OINTMENTS

UNGUENTUM.	INGREDIENTS.	STRENGTH.
Acidi Borici ..	Boric acid, white paraffin ointment.	10%.
Acidi Salicylici ..	Salicylic acid, white paraffin ointment.	2%.
Acidi Tannici ..	Tannic acid, glycerin, yellow beeswax, benzoinated lard.	20%.

OINTMENTS—*continued*

UNGUENTUM.	INGREDIENTS.	STRENGTH.
Aquosum	Borax, white beeswax, olive oil, white soft paraffin, water.	24% water.
Capsici	Capsicum, hard and soft paraffin, lard.	25%.
Chrysarobini ..	Chrysarobin, simple ointment.	4%.
Hamamelidis	Liquid extract of hamamelis, wool fat soft paraffin.	10% Liquid Extract.
Hydrargyri ..	Mercury, benzoinated lard, suet.	30%.
Hydrargyri Dilutum	Ointment of mercury, simple ointment.	33·3% Ung. Hydrarg.
Hydrargyri Ammoniati	Ammoniated mercury, simple ointment.	5%.
Hydrargyri Comp.	Mercury ointment, yellow beeswax, olive oil, camphor.	40% Ung. Hydrarg.
Hydrargyri Nitratis Forte	Mercury, nitric acid, lard, olive oil.	6·7% Hg equivalent.
Hydrargyri Nitratis Dilutum	Mercuric nitrate ointment, soft paraffin.	20% Ung. Hyd. Nit
Hydrargyri Oleati ..	Oleated mercury, simple ointment.	25%.
Hydrargyri Subchloridi	Calomel, simple ointment.	20%.
Paraffini	White beeswax, hard paraffin, white or yellow soft paraffin.	—
Phenolis	Phenol, hard and white soft paraffin, white beeswax, lard.	3%.
Simplex	Wool fat, hard and white or yellow soft paraffin.	—
Sulphuris	Sublimed sulphur, simple ointment.	10%.
Zinci Oleati	Freshly prepared zinc oleate, white soft paraffin.	50% oleate.
Zinci Oxidi	Zinc oxide, simple ointment.	15%.

Vaccinum Typho-paratyphosum—Anti-typhoid-paratyphoid Vaccine.—This is a sterile suspension of micro-organisms containing, in 1 mil, 1,000 million *Bacillus typhosus*, 500 million *Bacillus paratyphosus* A, and 500 million *Bacillus paratyphosus* B, which have been killed by heat. *Dose*—By subcutaneous injection, 0·5 mil (first dose), 1·0 mil (second dose after 7 to 10 days' interval).

Vaccinum Vacciniæ—Vaccine Lymph.—Vaccine lymph is a preparation of the substance which is obtained from the vesicles produced by inoculation of vaccinia virus on the skin of healthy animals. The containers should be glass capillary tubes of a size sufficient to hold one human dose; containers to hold several doses may be used in an emergency. *Dose*—By scarification, 1 min. (0·06 mil).

ALTERNATIVE PREPARATIONS SANCTIONED BY THE B.P. FOR USE IN TROPICAL AND SUBTROPICAL PARTS OF THE BRITISH EMPIRE.

Aurantii Cortex.—In parts of the Empire where bitter oranges cannot be obtained, either dried bitter-orange peel or fresh sweet-orange peel may be used in preparing Tincture of Orange.

Emplastra.—In tropical and subtropical parts of the Empire, more or less hard soap, colophony, or yellow beeswax may be employed in the preparation of the Plasters of the Pharmacopœia, when prevailing high temperatures otherwise render the basis too soft for convenient use ; but the official proportion of the active ingredient must in all cases be maintained.

Extracta Liquida.—Any Liquid Extract, defined in the Text of the Pharmacopœia, containing less than 30% v/v of ethyl alcohol, may have the proportion of ethyl alcohol increased to an amount not exceeding 30% v/v of the extract, in tropical and subtropical parts of the Empire where otherwise the preparation would be liable to ferment.

Limonis Cortex Siccatus.—In tropical and subtropical parts of the Empire, when fresh lemon peel cannot be obtained, dried lemon peel may be used in preparing Concentrated Compound Infusion of Gentian, Fresh Compound Infusion of Gentian, Syrup of Lemon, and Tincture of Lemon.

Oleum Olivæ.—In parts of the Empire, other than the United Kingdom and the Irish Free State, where Olive Oil is not readily obtainable, Arachis Oil or Sesame Oil, but no other oil or fat, may be employed in place of Olive Oil in making the official Liniments, Plasters, Ointments, and Soaps for which Olive Oil is directed to be used.

Unguenta.—In tropical and subtropical parts of the Empire more or less benzoinated lard, lard, suet, yellow beeswax, or white beeswax, may be employed in the preparation of the Ointments of the Pharmacopœia when prevailing high temperatures otherwise render the basis too soft for convenient use ; but the official proportion of the active ingredient must in all cases be maintained.

CHANGES IN COMPOSITION OF OFFICIAL REMEDIES IN CONSEQUENCE OF THE WAR.

Changes have been introduced in the composition of official preparations, due to the importance of conserving supplies of

certain substances—notably oil, glycerin and sugar. These changes have been notified in the 2nd, 3rd, and 4th Addenda to the Pharmacopœia, and are detailed below.. The new preparations and substances introduced by these Addenda are incorporated in Chapter XVI and the Materia Medica.

1. Substitution of Arachis, Cotton seed or Sesame oil for Olive Oil—
   Linimentum Camphoræ, Unguentum Aquosum, Unguentum Hydrargyri Compositum.

2. Substitution of Arachis Oil for Olive Oil—
   Emplastrum Plumbi, Injectio Bismuthi Salicylatis, Injectio Hydrargyri, Injectio Hydrargyri Subchloridi Unguentum Hydrargyri, Nitratis Forte.

3. To conserve glycerin supplies—
   (*a*) It may be omitted in Tinctura Cardamomi Composita, Tinct. Ipecacuanhae, Tinct. Rhei Composita, Ung. Acidi Tannici (new formula), Glycerinum Acidi Tannici (contains no Glycerin), Mel Boracis, Cataplasma Kaolini (Glycerin replaced by 70 per cent. Sodium Lactate), Syrupus Pruni Serotinae (Glycerin and sucrose may be omitted and replaced by tragacanth mucilage and saccharin), and Elixir Cascarae Sagradae.

4. Substitution of Sodium and Ammonium salts, for Potassium and Magnesium salts—
   Glycerinum Aluminis (Ammonium Alum instead of the Potassium salt), Mistura Sennae Composita (Sodium sulphate instead of Magnesium sulphate).

5. Use of tap water instead of distilled water—
   A large number of aromatic waters, fresh and concentrated in fusions, and Dakin's solution.

6. Other substitutions—
   Indian Squill may be used instead of Squill, and Indian Valerian instead of Valerian; Synthetic menthol instead of natural; Simple ointment in the preparation of Ung. Capsici.

SECTION III

MATERIA MEDICA

In consequence of the war, many substances, which were formerly manufactured only in Germany, are now made in this country. The Second, Third, and Fourth Addenda to the Pharmacopœia have included a number of these compounds and given them official Pharmacopœial names. These are shown in the table below, together with the proprietary name by which the compound was formerly known.

The Pharmacopœia Commission has published a list of compounds which are to be included in the Pharmacopœia at a later date. For these compounds, the Commission has suggested names, which it hopes will be generally adopted. These names are also set out in the table below in the third column.

FORMER TRADE NAME.	OFFICIAL NAME.	APPROVED NAME
Atebrin	Mepaerine Hydrochloride	—
Atebrin Musonate	Mepaerine Methane sulphonate	—
Avertin	Bromethol	—
Cardiazol	Leptazol	—
Coramine	Nikethamide	—
Doryl	Carbachol	—
Evipan	Hexobarbitone	—
Evipan-Sodium	Soluble Hexobarbitone	—
Fouadin	Stibophen	—
Germanin (Bayer "205")	Suramin	—
Plasmoquin	Pamaquin	—
Prominal	Phemitone	—
Uroselectan-B	Iodoxyl	—
Albucid	—	Sulphacetamide
Benzedrine	—	Amphetamine
Cignolin	—	Dianthrol

FORMER TRADE NAME	OFFICIAL NAME	APPROVED NAME
Cortenil	—	Percortin
Decicaine	—	Amethocaine
Dolantil	—	Pethidine Hydrochloride
Epanutin	—	Eptoin
Esmodil	—	Meprochol
Mitigal	—	Sudermo
Per-Abrodil	—	Pylumbrin
Phanodorm	—	Cyclobarbitone
Veritol	—	Pholandrene

This Materia Medica Section has been enlarged by the addition of monographs on the newer substances, mentioned by the official name in the middle column of this table, and many other compounds included in the 2nd, 3rd, and 4th Addenda to the Pharmacopœia, together with Sulphacetamide (*Albucid*) and Amphetamine (*Benzedrine*) and various other drugs considered of importance.

ACACIA (Acaciæ Gummi; Gum Acacia).

The dried gummy exudation from the stem and branches of *Acacia senegal* Willd. and other species of acacia.

CHARACTERS.

Rounded or ovoid tears, nearly colourless to pale yellow. Usually dispensed in the form of a white impalpable powder.

USES.

Demulcent. The mucilage is used in the dispensing of resinous tinctures, while the powder is used in the preparation of emulsions.

PREPARATIONS.

Injectio Sodii Chloridi et Acaciæ, B.P.—A solution of 9 gm. of sodium chloride and 60 gm. of acacia tears in freshly distilled water is made up to 1000 mils. The solution is heated in an autoclave at 121 to 122° C. for one hour. The liquid is strained through cotton wool, filtered through alternate layers of filter paper and linen, distributed into its final container and autoclaved. Used as an intravenous injection in cases of severe hæmorrhage to raise and maintain the blood pressure.

Mucilago Acaciæ, B.P.—A viscid liquid, prepared by dissolving 400 gm. of acacia tears, after rinsing, in 600 mils of chloroform water.

ACETANILIDUM (Acetanilide).

SYNONYM.

Antifebrin.

CHARACTERS.

Colourless, odourless, glittering crystals, with a burning taste.

Soluble 1 in 210 parts of water.

USES.

Antipyretic and analgesic.

Caution.—The formation of methæmoglobin and consequent cyanosis may occur from large or continuous doses.

DISPENSING.

Administered as a powder, in cachets or as tablets. When dispensed in a mixture it should be suspensed with Pulv. Trag. Co.

DOSE.

2 to 5 gr. (0·12 to 0·3 gm.).

PREPARATIONS.

Tabellæ Acetanilidi Compositæ, B.P.C. (Tab. Acetanilid. Co.).—Compound Tablets of Acetanilide. Each tablet contains 2 gr. of acetanilide, ½ gr. of caffeine and 1 gr. of sodium bicarbonate. *Dose*—1 or 2 tablets.

Tabellæ Acetanilidi Compositæ cum Codeina, B.P.C. (Tab. Acetanilid. Co. c. Codein.).—Compound Tablets of Acetanilide with Codeine. Each tablet contains 2 gr. of acetanilide, ½ gr. of caffeine, 1 gr. of sodium bicarbonate and ⅙ gr. of codeine. *Dose*—1 or 2 tablets.

ACETYLCHOLINA (Acetylcholine).

CHARACTERS.

A white crystalline, hygroscopic powder. Mostly used as acetylcholine chloride or bromide. Soluble in water.

USES.

Powerful vasodilator. Employed in Raynaud's disease, paralytic ileus and arterial hypertension. Injected subcutaneously or intramuscularly, ineffective orally.

CAUTION.

Intravenous injection may be dangerous.

DISPENSING.

Usually dispensed as a dry sterile powder in sealed ampoules. The powder is dissolved in sterile distilled water immediately before use.

DOSE.

$\frac{1}{3}$ to 3 gr. (0·02 to 0·2 gm.). By subcutaneous or intramuscular injection.

ACIDUM ACETYLSALICYLICUM (Acetylsalicylic Acid).

SYNONYM.

Aspirin.

CHARACTERS.

A white crystalline powder, or colourless acicular crystals, odourless and with a slightly acid taste. Stable in dry air, but moisture slowly hydrolyses it into acetic and salicylic acids.

STORAGE.

In well-stoppered bottles in a cool place.

USES.

Antipyretic, antirheumatic and analgesic.

DISPENSING.

When the powder is dispensed in a mixture, it must be suspended by means of Compound Powder of Tragacanth or Mucilage of Tragacanth. The acid can be dispensed in solution by dissolving with the aid of potassium citrate or ammonium acetate solution. It is also administered in cachets, powders and tablets.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

PREPARATIONS.

Haustus Acidi Acetylsalicylici Compositæ, B.P.C.—"A.P.C." Mixture. Acetylsalicylic acid, 5 gr.; phenacetin, 5 gr.; caffeine, $2\frac{1}{2}$ gr.; compound powder of tragacanth, 10 gr.; chloroform water to 1 fl. oz. *Dose*—1 fl. oz. (30 mils).

Mistura Acidi Acetylsalicylici, B.P.C. (Mist. Acid. Acetylsalicyl.).—Mixture of Acetylsalicylic Acid. *Syn.*—Aspirin Mixture. Each fluid ounce contains 15 gr. of acetylsalicylic acid with compound powder of tragacanth and chloroform water. *Dose*—$\frac{1}{2}$ to 1 fl. oz. (15 to 30 mils).

Tabellæ Acidi Acetylsalicylici Compositæ, B.P.C. (Tab. Acid. Acetylsalicyl. Co.).—Compound Tablets of Acetylsalicylic Acid. *Syn.*—Compound Aspirin Tablets. Each tablet contains $3\frac{1}{2}$ gr. of acetylsalicylic acid, $2\frac{1}{2}$ gr. of phenacetin and $\frac{1}{2}$ gr. of caffeine. *Dose*—1 or 2 tablets.

Tabellæ Acidi Acetylsalicylici et Opii, B.P.C. (Tab. Acid. Acetylsalicyl. et Opii).—Tablets of Acetylsalicylic Acid and Opium. *Syn.*—Tablets of Aspirin and Dover's Powder. Each tablet contains $2\frac{1}{2}$ gr. of acetylsalicylic acid and $2\frac{1}{2}$ gr. of powder of ipecacuanha and opium. *Dose*—1 to 3 tablets.

Proprietary Names.—Aspro (*Gollin, Slough*), Empirin (*Burroughs Wellcome, London*), and Genasprin (*Genatosan, Loughborough*) are names for acetylsalicylic acid in tablet form.

ACIDUM ASCORBICUM (Ascorbic Acid).

SYNONYMS AND PROPRIETARY NAMES.

Vitamin C, Redoxon (*Hoffman-La Roche, London*), Cantan (*Bayer Products, London*), Planavit C (*May & Baker, London*), Celin (*Glaxo, London*).

CHARACTERS.

Minute, colourless crystals, with an acid taste.
Readily *soluble* in water.

USES.

Used in the prophylaxis and treatment of scurvy.

STORAGE.

Decomposes in alkaline solution.

DISPENSING.

Usually administered in tablets or by intravenous injection, when the powder is dissolved in sterile distilled water.

DOSE.

Prophylactic (daily), $\frac{2}{5}$ to $\frac{4}{5}$ gr. (0·025 to 0·5 gm.); therapeutic (daily), $1\frac{1}{2}$ to 4 gr. (0·1 to 0·25 gm.).

ACIDUM BENZOICUM (Benzoic Acid).

CHARACTERS.

White, light feathery crystals; almost odourless, subliming on heating.

Soluble 1 in 450 parts of water and 1 in 3 parts of alcohol.

USES.

Antiseptic. Taken internally it is secreted as hippuric acid and decreases the alkalinity and bacterial content of the urine.

DISPENSING.

When prescribed in mixtures the acid should be suspended. Also prescribed in pills and lozenges.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

PREPARATIONS.

Trochisci Acidi Benzoici, B.P.C. (Troch. Acid. Benz.).—Benzoic Acid Lozenges. Each lozenge contains ½ gr. of benzoic acid. Expectorant and antiseptic.

Unguentum Acidi Benzoici Compositum, B.P.C. (Ung. Acid. Benz. Co.).—Compound Benzoic Acid Ointment. *Syn.*—Whitfield's Ointment. Benzoic acid, 5%, and salicylic acid, 3%, in white soft paraffin and coconut oil. For the treatment of ringworm.

ACIDUM BORICUM (Boric Acid).

SYNONYM.

Boracic Acid.

CHARACTERS.

White crystals or powder.

Soluble 1 in 25 parts of water, 1 in 3 parts of boiling water, and 1 in 5 parts of glycerin.

DISPENSING.

As a lotion, a solution in water is better prepared from the crystals. The acid is dispensed in fine powder, when used as an ingredient in an ointment or dusting powder.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

USES.

Boric acid is used as a mild antiseptic.

PREPARATIONS.

Glycerinum Acidi Borici (31%).—Glycerin of Boric Acid. *Dose*—10 to 30 min. (0·6 to 2·0 mils).

Lotio Acidi Borici, B.P.C. (Lot. Acid. Boric.).—Boric Acid Lotion. Boric acid, 1 in 30, in distilled water.

Unguentum Acidi Borici (10%).—Ointment of Boric Acid. 1 part of finely powdered boric acid with 9 parts of white paraffin ointment.

ACIDUM CITRICUM (Citric Acid).

CHARACTERS.

Colourless, prismatic crystals, or as a white powder.

Soluble 10 in 6 parts of water.

DISPENSING.

The powder is often directed to be added to a mixture containing alkali carbonate. The resulting mixture is then taken as an effervescing draught.

17 gr. dissolved in ½ oz. of water are equivalent to one tablespoonful of fresh lemon-juice in citric acid value, and will saturate in an effervescing mixture,

24½ gr. of potassium bicarbonate in 1 oz. water.
20 gr. of potassium carbonate in 1 oz.
35 gr. of sodium carbonate in 1 oz. water.
20½ gr. of sodium bicarbonate in 1 oz. water.
13 gr. of ammonium carbonate in 1 oz. water.

DOSE.

5 to 30 gr. (0·3 to 2 gm.).

ACIDUM HYDROCHLORICUM (Hydrochloric Acid).

CHARACTERS.

A solution of hydrogen chloride gas on water. Strength 32 per cent. w/w.

Caustic. Not used internally in this form.

PREPARATION.

Acidum Hydrochloricum Dilutum, B.P. (10% w/w of Hydrogen Chloride).—A colourless mixture of hydrochloric

acid and distilled water. *Dose*—5 to 20 min., in water (3 to 12 decimils).

ACIDUM HYDROCYANICUM DILUTUM (Dilute Hydrocyanic Acid) 2%.

SYNONYM.
Dilute Prussic Acid.

CHARACTERS.
A colourless liquid with powerful, characteristic odour.

STORAGE.
Small, glass-stoppered bottles, inverted in a cool place.

USES.
Sedative action on stomach. Often combined with bismuth carbonate or sodium bicarbonate in form of a mixture for this purpose. Allays vomiting and cough.

DOSE.
2 to 5 min. (0·12 to 0·3 mil).

ACIDUM MANDELICUM (Mandelic Acid).

CHARACTERS.
Colourless crystals with an acid taste.
Soluble 1 in about 8 parts of water.

USES.
To replace the ketogenic diet in the treatment of urinary infections. It exerts a bacteriostatic acid only when the urine is acid, and this is effected by the simultaneous administration of ammonium chloride (usually administered in capsules).

DISPENSING.
The acid is dispensed in mixture form either by dissolving in sodium bicarbonate solution with effervescence, or by the formation of ammonium mandelate from mandelic acid and strong solution of ammonia. The unpleasant taste is best disguised with liquid extract of liquorice, tincture of ginger and/or orange, with other flavouring agents.

DOSE.

45 gr. (3·0 gm.) in 1 fl. oz. of water, neutralized by sodium bicarbonate, four times a day.

PREPARATIONS.

Ammonii Mandelas.—Ammonium Mandelate. White, very hygroscopic crystals, *soluble* freely in water. Used to replace the combined treatment of sodium mandelate with ammonium chloride, and to avoid the administration of the nauseous ammonium chloride. Sometimes it is necessary to add ammonium chloride to obtain the desired acidity of urine. *Dose*—50 gr. (3·4 gm.) four times daily in solution.

Calcii Mandelas.—Calcium Mandelate. White, almost insoluble powder. Used as Ammonium Mandelate. May be suspended in mixtures; proprietary solutions are available (Mandecal, B.D.H.). *Dose*—50 gr. (3·0 to 4·0 gm.) four times daily in water.

Sodii Mandelas.—Sodium Mandelate. White crystalline compound. Soluble about 1 in $1\frac{1}{2}$ of water. Used as mandelic acid. *Dose*—50 gr. (3·4 gm.) four times daily.

ACIDUM NICOTINICUM (Nicotinic acid).

CHARACTERS.

White crystals or crystalline powder, odourless.

Soluble 1 in 75 of water, much more soluble in boiling water, and in boiling alcohol; soluble in alkalis; almost insoluble in ether.

USES.

Used in treatment of pellagra.

DOSE.

$\frac{3}{4}$ to $1\frac{1}{2}$ gr. (0·05 to 0·1 gm.).

PREPARATIONS.

Nicotinic Acid Amide (Nicotinamide).—Used for same purposes as nicotinic acid. *Dose*—about 5 gr. (0·3 gm.)

Pyridoxin (Vitamin B_6, Adermin).—Some evidence that it is of use in nutrition deficiency leading to muscular weakness. *Dose*—50 to 100 mgm., subcutaneously, each week.

ACIDUM SALICYLICUM (Salicylic Acid).

CHARACTERS.

Colourless crystals or light feathery powder. Sweetish taste.

Soluble 1 in 500 parts of water, 1 in 3·5 parts of alcohol %).

USES.

Antiseptic and antipruritic. Strong solutions destroy the epidermis.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

PREPARATIONS.

Amylum Salicylatum, B.P.C. (Amylum Salicylat.).—Salicylated Starch. Salicylic acid, 1 in 10, with starch.

Pulvis Zinci et Acidi Salicylici, B.P.C. (Pulv. Zinc. et Acid. Salicyl.).—Zinc and Salicylic Acid Powder. Zinc oxide, 20%, and salicylic acid, 5%, with starch.

Unguentum Acidi Salicylici, B.P.—Ointment of Salicylic Acid. 2% of salicylic acid in white paraffin ointment.

ACIDUM TANNICUM (Tannic Acid).

CHARACTERS.

Yellowish-white or light brown, glistening scales, or impalpable powder.

Soluble 1 in 1 part of water, 1 in 1 part of alcohol (90%), and 1 in 1 part of glycerin.

USES.

Used externally as a powerful astringent. A 2% solution is used for the treatment of burns. Suppositories of tannic acid are used as an astringent application to hæmorrhoids.

DISPENSING.

Incompatible with ferric salts (dark blue-black colour), acids, alkalis, silver salts, and gelatin. Precipitates alkaloids from solution.

PREPARATIONS.

Glycerinum Acidi Tannici, B.P.—Glycerin of Tannic Acid. Tannic acid, 15% in glycerin. *Dose*—10 to 30 min. (0·6 to 2·0 mils) (see page 303).

Lotio Acidi Tannici, B.P.C. (Lot. Acid. Tann).—Lotion of Tannic Acid. Tannic acid, 2%, and mercuric chloride, 1 in 2000, in distilled water. For the treatment of burns.

Suppositorium Acidi Tannici, B.P.—Tannic Acid Suppository. Each suppository contains 3 gr. of tannic acid.

Unguentum Acidi Tannici, B.P.—Ointment of Tannic Acid. Tannic acid, 20%, with glycerin, yellow beeswax and benzoated lard.

ACONITUM (Aconite).

The dried root of *Aconitum Napellus* Linn.

CONSTITUENTS.

Three alkaloids, aconitine, picraconitine and aconine.

USES.

Internally, the tincture is used as a febrifuge. Externally, the liniment is applied as an anodyne.

PREPARATIONS.

Linimentum Aconiti, B.P.—Liniment of Aconite. An alcoholic extract of aconite (1 in 2).

Linimentum Aconiti Oleosum, B.P.C. (Lin. Aconit. Oleos.).—Liniment of Aconite with Oil. *Syn.*—A.B.C. Liniment. Equal parts of Liniment of aconite, liniment of belladonna and liniment of chloroform. The non-oily liniment of the British Pharmaceutical Codex, 1923, is included under the name of Pigmentum Aconiti Compositum. This liniment should be well shaken before use as the oil in the chloroform liniment is not soluble in the other ingredients.

Tinctura Aconiti, B.P.C. (Tinct. Aconit.).—Tincture of Aconite. About 1 in 6. *Dose*—2 to 5 min. (0·12 to 0·3 mil).

ACRIFLAVINA (Acriflavine).

SYNONYM.

Flavine.

CHARACTERS.

A reddish-brown crystalline powder.

Soluble 1 in about 3 parts of water, 1 in 40 parts of alcohol, and 1 in 4 parts of glycerin.

Dilute solutions exhibit a green fluorescence.

USES.

Antiseptic. It has been stated that the bacteriostatic value is increased by the presence of serum. Usual strength 1 in 1000 in normal saline.

DISPENSING.

The solution or Emulsion of Acriflavine, B.P.C., is used as a general external antiseptic. Acriflavine can be incorporated in a pessary usually 1 in 500 parts of oil of theobroma or glycerin suppository base.

DOSE.

$\frac{1}{2}$ to $1\frac{1}{2}$ gr. (0·03 to 0·1 gm.).

PREPARATIONS.

Emulsio Acriflavinæ, B.P.C. (Emuls. Acriflavin.).—Emulsion of Acriflavine. Acriflavine, 1 in 1000, with liquid paraffin, white beeswax and distilled water (a w/o emulsion).

Liquor Acriflavinæ, B.P.C. (Liq. Acriflavin.).—Solution of Acriflavine. Acriflavine, 0·1% w/v, in physiological solution of sodium chloride.

ADEPS (Lard).

The purified internal fat of the hog.

SYNONYMS.

Adeps Præparatus, Prepared Lard.

CHARACTERS.

Soft, white unctuous fat.

USES.

Employed as an ointment base. More frequently used in the form of Adeps Benzoinatus, Benzoated Lard, the benzoin acts as an antiseptic and prevents the lard becoming rancid. Benzoinated lard is irritant and should not be used for application to the conjunctiva and other sensitive parts.

PREPARATION.

Adeps Benzoinatus, B.P.—Benzoinated Lard. Lard containing the fat-soluble portion from 3% of benzoin.

ADEPS LANÆ (Wool Fat).

Purified, anhydrous fat-like substance obtained from the wool of sheep.

SYNONYM.

Anhydrous Lanolin.

CHARACTERS.

Pale yellow, unctuous substance.

USES.

Not readily absorbed, but when mixed with olive oil or soft paraffin readily penetrates the skin. Takes up about 50% of water. Hydrous wool fat is more generally used as an ointment base; when mixed with lard, olive oil, etc., its stickiness is greatly reduced.

When phenol or mercuric chloride is to be combined in an ointment, use anhydrous wool fat in preference to the hydrous, since caustic action may result with the latter.

PREPARATION.

Adeps Lanæ Hydrosus, B.P.—Hydrous Wool Fat. *Syn.*—Lanolin. Wool fat with 30% of water.

ADRENALINA (Adrenaline).

SYNONYMS AND PROPRIETARY NAMES.

Adrenalin, Suprarenalin (*Armour, London*), Renaglandin (*Oppenheimer, London*), Paranephrin (*Merck, Darmstadt; Martindale, London*), Vasoconstrictine (*Duncan Flockhart, Edinburgh*).

The active principle of the suprarenal gland. May be obtained from the glands or prepared synthetically.

CHARACTERS.

A white or pale buff powder.

Soluble sparingly in water, readily in mineral acids and boric acid solution, forming corresponding salts.

USES.

Vasoconstrictor. Locally applied causes constriction of blood-vessels and blanching of the skin and mucous membrane. Thus used for checking capillary bleeding—e.g. after tooth extractions. Hypodermic injections are used to relieve asthmatic spasms. Intravenously it is useful in surgical shock and circulating failure. Intracardiac injection is employed in cases of heart failure and collapse under anæsthesia. It is often added to local anæsthetic solutions to prevent diffusion.

DISPENSING.

Dispensed in solution for injection as Liquor Adrenalinæ Hydrochloridi. As a spray in arachis oil or water, and as a suppository or ointment for use in hæmorrhoids.

DOSE.

$\frac{1}{600}$ to $\frac{1}{120}$ gr. (0·0001 to 0·0005 gm.).

PREPARATIONS.

Insufflatio Adrenalinæ, B.P.C. (Insuff. Adrenal.).—Adrenaline Insufflation. *Syn.*—Adrenaline Snuff. Adrenaline, about 1 in 1300, with boric acid, camphor, menthol, potassium chlorate, oil of eucalyptus and lycopodium.

Liquor Adrenalinæ Hydrochloridi, B.P.—Solution of Adrenaline Hydrochloride. A sterile preparation containing adrenaline 1 in 1000, dilute hydrochloric acid, chlorbutol and sodium chloride, in distilled water. Stored in well-filled, well-closed containers, away from the light. *Dose*—2 to 8 min. (0·12 to 0·5 mil).

Nebula Adrenalinæ et Ephedrinæ Oleosa, B.P.C. (Neb. Adrenal. et Ephed. Oleos.).—Oily Adrenaline and Ephedrine Spray. Adrenaline, 1 in 10,000, and ephedrine, 1 in 50, with menthol and eucalyptol in acidified dehydrated alcohol, castor oil and arachis oil.

Suppositorium Adrenalinæ, B.P.C. (Supp. Adrenal.).—Adrenaline Suppository. Each suppository contains $\frac{1}{60}$ gr. of adrenaline.

ALCOHOL (Alcohol 95%), C_2H_5OH.

Obtained by the distillation of fermented saccharine liquids and contains 94·7 to 95·2% v/v or 92 to 92·7% w/w of ethyl alcohol, C_2H_5OH.

CHARACTERS.

A colourless, transparent, mobile, volatile liquid, with a characteristic spirituous odour, burning taste.

Miscible in all proportions with water, ether, and chloroform. It is used in preparing the following dilute alcohols :

PREPARATIONS.

Alcohol (90%) v/v.—*Syn.*—Rectified Spirit, S.V.R. Dilute 948 mils (95%) to 1000 mils with distilled water, S.G. 0·832 to 0·835.

Alcohol (80%) v/v.—Dilute 842 mils (95%) to 1000 mils with distilled water, S.G. 0·863 to 0·865.

Alcohol (70%) v/v.—Dilute 737 mils (95%) to 1000 mils with distilled water, S.G. 0·889 to 0·891.

Alcohol (60%) v/v.—Dilute 632 mils (95%) to 1000 mils with distilled water, S.G. 0·913 to 0·914.

Alcohol (50%) v/v.—Dilute 526 mils (95%) to 1000 mils with distilled water, S.G. 0·934 to 0·935.

Alcohol (45%) v/v.—Dilute 474 mils (95%) to 1000 mils with distilled water, S.G. 0·943 to 0·944.

Alcohol (25%) v/v.—Dilute 263 mils (95%) to 1000 mils with distilled water, S.G. 0·970 to 0·971.

Alcohol (20%) v/v.—Dilute 210 mils (95%) to 1000 mils with distilled water, S.G. 0·975 to 0·976.

NOTE.—On mixing alcohol and water, contraction of volume and rise of temperature will occur. The temperature must be allowed to fall to about 15° before the final adjustment of volume is made.

ALOE (Aloes).

Aloes is the solid residue obtained by evaporating the liquid which drains from the transversely cut leaves of various species of *Aloe*.

CHARACTERS.

For dispensing purposes the drug is prepared in impalpable powder. It varies in colour from light to dark brown.

CONSTITUENTS.

Barbaloin, isobarbaloin, resin and aloeemodin.

USES.

Purgative. Rarely prescribed alone, since carminatives are required to moderate the tendency to griping. Valuable drug for treatment of constipation.

DOSE.

2 to 5 gr. (0·12 to 0·3 gm.).

PREPARATIONS.

Decoctum Aloes Compositum, B.P.C. (Dec. Aloes Co.).—Compound Decoction of Aloes. Aloes, 1% w/v, with myrrh, potassium carbonate, extract of liquorice, compound tincture of cardamom and distilled water. When Decoctum Aloes Compositum is prescribed, either this preparation, or Decoctum Aloes Compositum Concentratum diluted with three times its

volume of distilled water, may be dispensed. *Dose*—½ to 2 fl. ozs. (15 to 60 mils).

Pilula Aloes, B.P.—Pill of Aloes. Aloes, hard soap, oil of caraway and syrup of glucose. *Dose*—4 to 8 gr. (0·25 to 0·5 gm.).

Pilula Aloes et Ferri, B.P.—Pill of Aloes and Iron. Exsiccated Ferrous Sulphate and Aloes, with cinnamon, cardamom and ginger. *Dose*—4 to 8 gr. (0·25 to 0·5 gm.).

Pilula Aloes et Nucis Vomicæ, B.P.C. (Pil. Aloes et Nuc. Vom.)—Aloes and nux vomica Pills. Each pill contains 2 gr. of aloes, ¼ gr. of dry extract of nux vomica and ⅙ gr. of dry extract of belladonna. *Dose*—1 pill.

ALOINUM (Aloin).

A mixture of crystalline principles obtained from aloes.

CHARACTERS.

A pale yellow powder, with an intensely bitter taste.

USES.

Similar to aloes.

DOSE.

½ to 2 gr. (0·03 to 0·12 gm.).

PREPARATIONS.

Pilulæ Aloini Compositæ, B.P.C. (Pil. Aloin. Co.).—Compound Aloin Pills. *Syn.*—Andrew Clark's Liver Pills. Each pill contains ½ gr. each of aloin, dry extract of nux vomica, exsiccated ferrous sulphate, myrrh and hard soap. *Dose*—1 pill.

Pilulæ Phenolphthaleini Compositæ, B.P.C. (Pil. Phenolphthal. Co.).—Compound Phenolphthalein Pills. *Syn.*—Pilulæ Phenaloini. Each pill contains ¼ gr. of aloin, ½ gr. of phenolphthalein, $\frac{1}{50}$ gr. of strychnine, $\frac{1}{12}$ gr. of dry extract of belladonna and $\frac{1}{15}$ gr. of powdered ipecacuanha. *Dose*—1 or 2 pills.

Alophen Pill (*Parke Davis, London*), contains aloin, phenolphthalein, ipecacuanha, strychnine and extract of belladonna.

Tabellæ Aloini Compositæ, B.P.C. (Tab. Aloin Co.).—Compound Aloin Tablets. Each tablet contains ⅕ gr. of aloin, ¼ gr. of powdered ipecacuanha, and ⅛ gr. of dry extract of nux vomica. *Dose*—1 or 2 tablets.

AMETHOCAINUM HYDROCHLORIDUM (Amethocaine Hydrochloride).

SYNONYMS AND PROPRIETARY NAMES.

Decicaine (*Bayer Products, London*); Pantocaine, Anethaine (*Glaxo Laboratories, London*).

CHARACTERS.

A white crystalline powder, *soluble* about 1 in 7 of water, also *soluble* in alcohol.

USES.

Local anæsthetic. Often combined with adrenaline to localize effect and minimize toxic action.

AMIDOPYRINA (Amidopyrine).

SYNONYMS AND PROPRIETARY NAMES.

Amidofebrin, Pyramidon (*Bayer Products, London*).

CHARACTERS.

An odourless and colourless, crystalline powder.

Soluble 1 in about 18 parts of water.

USES.

Antipyretic and analgesic.

CAUTION.—Amidopyrine alone, or amidopyrine in combination with other substances, particularly barbiturates, may cause agranulocytosis.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

AMMONII CARBONAS (Ammonium Carbonate).

CHARACTERS.

Hard crystalline masses, with a strong odour of ammonia and a pungent ammoniacal taste.

Soluble 1 in 4 parts of water.

STORAGE.

In well-closed containers.

USES.

As a stimulant and expectorant. Often combined with ipecacuanha and senega.

DISPENSING.

The powder is unstable if the bottle is frequently opened. Use a solution of strength 1 in 8—this has been found to be stable.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

PREPARATIONS.

Mistura Ammoniæ cum Senegæ, B.P.C. (Mist. Ammon. c. Seneg.).—Ammonia Mixture with Senega. Each fluid ounce contains 4 gr. of ammonium carbonate and 5 gr. of ammonium chloride, with tincture of ipecacuanha and infusion of senega. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Spiritus Ammoniæ Aromaticus, B.P.—Aromatic Spirit of Ammonia. *Syn.*—Spirit of Sal Volatile. Prepared from ammonium carbonate, strong solution of ammonia, oil of lemon, oil of nutmeg, alcohol and distilled water. *Dose*—¼ to 1 fl. dr. (1 to 4 mils).

AMMONII CHLORIDUM (Ammonium Chloride).

CHARACTERS.

White granular crystalline powder.

Soluble 1 in 3 parts of water.

USES.

Mildly expectorant, diaphoretic and diuretic. Given by mouth increases the acidity of the urine.

DISPENSING.

In mixtures, tablets and lozenges, liquorice is often used to disguise the taste.

DOSE.

5 to 60 gr. (0·3 to 4 gm.).

AMYLIS NITRIS (Amyl Nitrite).

CHARACTERS.

A clear yellow liquid with a fragrant odour and an aromatic pungent taste. Inflammable and very volatile.

Insoluble in water; *miscible* with alcohol and ether.

USES.

Dilates the blood vessels and lowers the blood pressure. Mainly used for the relief of attacks of angina pectoris, acting by dilatation of the coronary artery.

DISPENSING.

Thin glass capsules encased in cotton wool and silk. The capsule is broken and the vapour cautiously inhaled.

DOSE.

2 to 5 min. (0·12 to 0·3 mils).

AMYLOCAINÆ HYDROCHLORIDUM (Amylocaine Hydrochloride).

PROPRIETARY NAME.

Stovaine (*May & Baker London*).

CHARACTERS.

A colourless, crystalline powder, with a bitter taste.

Soluble 1 in 2 parts of water, 1 in 3 parts of dehydrated alcohol.

USES.

Local anæsthetic.

DISPENSING.

A solution for injection may be sterilized by heating with a bactericide or filtration. Glass containers should be free from alkali. Dispensed in ointment for painful wounds and hæmorrhoids.

DOSE.

$\frac{1}{3}$ to $\frac{3}{4}$ gr. (0·02 to 0·05 gm.) by mouth or by subcutaneous injection ; $\frac{1}{2}$ to $1\frac{1}{2}$ gr. (0·02 to 0·1 gm.) by intrathecal injection.

PREPARATION.

Unguentum Adrenalinæ et Amylocainæ Compositum, B.P.C. (Ung. Adrenal. et Amylocain. Co.).—Compound Ointment of Adrenaline and Amylocaine. Adrenaline, 1 in 14,000, as benzoate, amylocaine hydrochloride and benzocaine, of each 1%, and liquid extract of hamamelis, 7·5% v/w, in wool fat and yellow soft paraffin.

AMYLUM (Starch).

CHARACTERS.

A fine white odourless and tasteless powder.

USES.

As a dusting powder for applications to chafings, it is used alone or mixed with zinc oxide, boric acid, etc. The mucilage is the basis for many enemata. Glycerin Amyli is a protective application for skin diseases.

PREPARATIONS.

Glycerinum Amyli, B.P.—Glycerin of Starch. Starch is heated with glycerin and water until gelatinized.

Pulvis Zinci et Amyli, B.P.C. (Pulv. Zinc. et Amyli).—Zinc and Starch Powder. Equal parts of zinc oxide and starch.

Pulvis Zinci et Amyli Compositus, B.P.C. (Pulv. Zinc. et Amyli Co.).—Compound Zinc and Starch Powder. Equal parts of zinc oxide, starch, boric acid and purified talc, perfumed with oil of geranium.

ANETHUM (Dill).

The dried ripe fruits of *Anethum graveolens* Linn. They contain 3 to 4% of volatile oil.

USES.

Carminative. It is used in mixtures in the form of Aqua Anethi, which is a common domestic remedy for flatulence of infants.

PREPARATION.

Aqua Anethi Destillata.—Distilled Dill Water. A colourless liquid, prepared by distilling 10 parts from 1 of dill fruit and 20 of water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

ANTIMONII ET POTASSII TARTRAS (Potassium Antimonyl Tartrate).

SYNONYMS.

Antimonium Tartratum, Tartar Emetic, Tartrated Antimony, Antimony and Potassium Tartrate.

CHARACTERS.

Colourless crystals, or white granular powder.
Soluble 1 in 17 parts of water.

USES.

Diaphoretic and emetic when given orally. It is injected intravenously in the treatment of certain tropical diseases, leishmaniasis, trypanosomiasis, frambœsia, bilharziasis and filariasis.

DISPENSING.

Solutions for injection can be sterilized by heating in an autoclave or filtration. It is given orally in mixtures as Vinum Antimoniale. Incompatible with acids and alkalis, soap and tannin.

DOSE.

$\frac{1}{32}$ to $\frac{1}{8}$ gr. (0·002 to 0·008 gm.); $\frac{1}{2}$ to 1 gr. (0·03 to 0·06 gm.) as emetic; $\frac{1}{2}$ to 2 gr. (0·3 to 0·12 gm.) by intravenous injection.

PREPARATION.

Vinum Antimoniale, B.P.C. (Vin. Antim.):—Antimonial Wine. Potassium antimonyltartrate, 0·4% w/v, in sherry-type wine. *Dose*—10 to 30 min. (0·6 to 2 mils); 2 to 4 fl. dr. (8 to 16 mils) as emetic.

ANTIMONII ET SODII TARTRAS (Sodium Antimonyltartrate).

CHARACTERS.

Colourless, hygroscopic scales or as a powder.
Soluble 1 in $1\frac{1}{2}$ parts of water.

USES.

Similar to potassium antimonyl tartrate. Less toxic and more soluble.

DISPENSING.

Solutions for injection may be sterilized by heating in an autoclave or filtration.

DOSE.

$\frac{1}{32}$ to $\frac{1}{8}$ gr. (0·002 to 0·008 gm.); $\frac{1}{2}$ to 1 gr. (0·03 to 0·06 gm.) as an emetic; $\frac{1}{2}$ to 2 gr. (0·03 to 0·12 gm.) by intravenous injection.

ANEURINÆ HYDROCHLORIDUM (Aneurine hydrochloride).

SYNONYMS.

Aneurine Chloride Hydrochloride, Vitamin B_1, Thiamine Hydrochloride.

CHARACTERS.

Colourless crystalline substance.

Soluble about 1 in 1 of water, *insoluble* in oils and ether.

USES.

Used in treatment of beri-beri, and polyneuritis. Normal daily requirements about 1 to 2 mgm. (300 to 600 units).

DISPENSING.

Solution may be sterilized by autoclaving if *p*H less than 5·5. Protect solution from light on storage. Neutral and alkaline solutions deteriorate rapidly, especially in contact with air.

DOSE.

Prophylactic (daily) $\frac{1}{200}$ to $\frac{1}{100}$ gr. (0·0003 to 0·0006 gm.); 100 to 200 units.

Therapeutic (daily) $\frac{1}{100}$ to $\frac{1}{33}$ gr. (0·0006 to 0·0018 gm.); 200 to 600 units.

PREPARATION.

Pulvis Vitamin B_1 (Adsorbate of Vitamin B_1).—An adsorbate of antineuritic vitamin (Vitamin B_1) on fuller's earth. One gramme contains 100 units of anti-neuritic activity. Used therapeutically and prophylactically in beri-beri. *Dose*—Prophylactic (daily) 15 to 30 gr. (1 to 2 gm.); Therapeutic (daily) 30 to 90 gr. (2 to 6 gm.).

AMPHETAMINÆ SULPHAS (Amphetamine Sulphate).

PROPRIETARY NAME.

Benzedrine Sulphate (*Menley & James, London*).

CHARACTERS.

A white powder, odourless, bitter taste.

Soluble freely in water, slightly in alcohol.

USES.

Powerful stimulant for central nervous system.

DOSE.

$\frac{1}{24}$ to $\frac{1}{6}$ gr. (0·0025 to 0·01 gm.).

APOMORPHINÆ HYDROCHLORIDUM (Apomorphine Hydrochloride).

CHARACTERS.

Small greyish-white crystals, turning green on exposure to light and air.

Soluble 1 in 50 parts of water, 1 in 50 parts of alcohol.

USES.

Powerful emetic; rapid emesis produced by injection. Taken by mouth as an expectorant.

DISPENSING.

Apomorphine hydrochloride is incompatible with alkaline substances.

Sterilize solutions by heating with a bactericide or filtration. Solutions should contain 0·05% Sodium metabisulphite. Decomposition may give rise to toxic solutions, and solutions which become green should be rejected. Use alkali-free containers.

DOSE.

Expectorant, $\frac{1}{64}$ to $\frac{1}{32}$ gr. (0·001 to 0·002 gm.); emetic or hypnotic, $\frac{1}{32}$ to $\frac{1}{8}$ gr. (0·002 to 0·008 gm.) by subcutaneous injection.

PREPARATION.

Syrupus Apomorphinæ, B.P.C. (Syr. Apomorph.).—Syrup of Apomorphine. Each fluid drachm contains $\frac{1}{36}$ gr. of apomorphine hydrochloride with dilute hydrochloric acid, alcohol (90%), distilled water and syrup. *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils). Used as an expectorant.

ARGENTI NITRAS (Silver Nitrate).

CHARACTERS.

Colourless, odourless transparent crystals.

Soluble 2 in 1 part of water, 1 in 25 parts of alcohol.

USES.

Caustic and astringent. Destroys warts and other skin growths. Internally, has been used for dyspepsia, vomiting and diarrhœa.

DISPENSING.

Incompatible with alkalis, halogen acids and salts, hydrocyanic acid and salts. As a lotion for wounds or ulcers, 10 grains to the fluid ounce. As a lotion for ophthalmia in infants, 4 gr. to the fluid ounce. As an injection for the urethra, 2 gr. to the fluid ounce. Internally administered in pills, which should be massed with wool fat and kaolin.

DOSE.

$\frac{1}{8}$ to $\frac{1}{4}$ gr. (0·008 to 0·016 gm.) (in pill form).

ARGENTI PROTEINAS MITE (Mild Silver Proteinate).

SYNONYMS AND PROPRIETARY NAMES.

Silver Nucleinate, Silver Nitellin, Argyrol (*Fassett & Johnson, London*), Arvitin (*Johnson & Sons, London*), Cargentos (*Sharp & Dohme, London*), Lunargen (*Lilly, London*).

CHARACTERS.

A brown powder, scales or granules.

Soluble in water.

NOTE.—This preparation contains more silver than the strong silver protein compounds, yet is designated Mild Silver Protein because it is less irritant.

USES.

A mild antiseptic, used where it is important to avoid irritation.

ARGENTOPROTEINUM (Silver Protein).

SYNONYMS AND PROPRIETARY NAMES.

Strong Silver Protein, Silver Proteinate, Argein (*Allen & Hanburys, London*), Protargol (*Bayer Products, London*).

CHARACTERS.

A light brown powder, somewhat hygroscopic.

Soluble about 1 in 2 of water.

DISPENSING.

Solutions are best prepared by shaking the powder on to the surface of cold water. Should be dispensed in amber bottles.

STORAGE.

In well-closed containers, protected from light.

USES.

A mild antiseptic, free from the corrosive and astringent properties of silver nitrate.

ARSENII TRIIODIDUM (Arsenic Triiodide).

CHARACTERS.

Small orange-red crystals.

Soluble 1 in 18 parts of water.

USES.

In diseases of the alimentary canal—gastritis.

DOSE.

$\frac{1}{16}$ to $\frac{1}{4}$ gr. (0·004 to 0·016 gm.).

PREPARATION.

Liquor Arseni et Hydrargyri Iodidi.—Solution of Arsenious and Mercurous Iodides. *Syn.*—Donovan's Solution. A clear, pale yellow liquid. *Uses*—Syphilitic skin diseases. *Dispensing*—Incompatible with alkaloids ; preferably administered alone. *Dose*—5 to 15 min. (0·3 to 1·0 mil).

ARSENII TRIOXIDUM (Arsenic Trioxide).

SYNONYMS.

Arsenic, Arsenious Oxide, Arsenious Anhydride, Arsenious Acid.

CHARACTERS.

Heavy white powder, or vitreous masses.

Soluble, in water slowly, 1 in 65 ; in glycerin, 1 in 8.

USES.

General and nerve tonic. Given for psoriasis and eczema.

DISPENSING.

Usually administered in solution as Liquor Arsenicalis. Given as oxide in pills. Administered after meals.

DOSE.

$\frac{1}{60}$ to $\frac{1}{12}$ gr. (0·001 to 0·005 gm.).

PREPARATION.

Liquor Arsenicalis.—Solution of Arsenic. *Syn.*—Liquor

Arsenicalis seu Fowleri; Fowler's Solution. A neutral solution of arsenic trioxide. *Dose*—2 to 8 min. (0·12 to 0·5 mil).

This is the most frequently used preparation of arsenic, and, like all the preparations of the drug, should be commenced in small doses and gradually increased. A good rule is to begin in adults with 2 min. and gradually increase to 8 or more—always after meals, and freely diluted. Children bear as large doses as adults.

ASAFŒTIDA (Asafetida).

The fetid oleo-gum-resin, obtained by incisions from the root of *Ferula fœtida* Regel and probably other species.

CHARACTERS.

Irregular softish masses or tears of a dull yellow colour, which darken on keeping.

USES.

Carminative and antispasmodic.

DISPENSING.

Usually given in mixtures in the form of the tincture, which requires suspension with mucilage when mixed with solutions of electrolytes. Asafœtida itself forms an emulsion when triturated with water.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

PREPARATIONS.

Pilula Aloes et Asafœtida.—Pill of Aloes and Asafœtida. Cathartic and antispasmodic. *Dose*—4 to 8 gr. (0·25 to 0·5 gm.).

Tinctura Asafœtida.—*Dose*—½ to 1 fl. dr. (2 to 4 mils).

ATROPINA (Atropine).

CHARACTERS.

Colourless crystals.

Soluble 1 in 500 parts of water.

USES.

Local anodyne and mydriatic.

DOSE.

$\frac{1}{240}$ to $\frac{1}{60}$ gr. (0·00025 to 0·001 gm.).

PREPARATIONS.

Atropinæ Sulphas.—Atropine Sulphate. Nearly colourless crystals. *Soluble* 1 in 1 part of water and 1 in 4 parts of alcohol (90%). *Uses*—Employed in making hypodermic solutions, eye drops and other preparations of atropine. Solutions for injection are sterilized by filtration, and by heating with a bactericide, all glass containers should be alkali-free. *Dose*—$\frac{1}{240}$ to $\frac{1}{60}$ gr. (0·00025 to 0·001 gm.).

Oculentum Atropinæ.—Atropine Eye Ointment. Contains 0·25% atropine sulphate.

Oculentum Atropinæ cum Hydrargyri Oxido.—Contains 0·125% atropine sulphate and 1% yellow mercuric oxide.

AURANTII CORTEX SICCATUS (Dried Bitter Orange Peel).

The dried outer part of the ripe or nearly ripe fruits of *Citrus Aurantium* Linn.

USES.

Valuable aromatic, bitter or flavouring agent.

PREPARATIONS.

Infusum Aurantii Concentratum.—Prepared by macerating dried bitter-orange peel in alcohol (25%). When diluted 1 in 8 with distilled water, it yields a preparation approximately equivalent in strength, but not in flavour, to Inf. Aurant. Recens, and contains a little alcohol.

Infusum Aurantii Recens.—Fresh Infusion of Orange Peel. Dried bitter-orange peel infused in boiling water. *Dose*—$\frac{1}{2}$ to 1 oz. (15 to 30 mils). For dispensing purposes, this fresh infusion must be used within 12 hours of its preparation.

NOTE.—The prescriber must specify Inf. Aurant. *Recens* on the prescription if he wishes the fresh infusion to be dispensed.

Syrupus Aurantii (1 in 8).—1 of tincture of orange and 7 of syrup, mixed. *Dose*—$\frac{1}{2}$ to 2 dr. (2 to 8 mils).

Tinctura Aurantii (25%).—Prepared by macerating fresh bitter-orange peel in alcohol (90%). An agreeable Bitter Tonic and flavouring agent. *Dose*—$\frac{1}{2}$ to 1 dr. (2 to 4 mils). In Conf. Sulphuris, Syr. Aurant.

BALSAMUM PERUVIANUM (Balsam of Peru).

A dark, viscid liquid balsam, exuded from the trunk of *Myroxylon Pereiræ* (Royle) Klotzsch after the bark has been beaten and scorched.

USES.

Expectorant.. Used externally as an antiseptic and parasiticide, especially in scabies.

DISPENSING.

Applied in the form of an ointment. Internally, requires mucilage of acacia when mixed with water.

DOSE.

5 to 15 min. (0·3 to 1 mil).

PREPARATION.

Unguentum Zinc cum Balsamo Peruviano, B.P.C. (Ung. Zinc. c. Bals. Peruv.).—Zinc Ointment with Balsam of Peru. Balsam of Peru, about 11%, in ointment of zinc oxide and ointment of boric acid.

BALSAMUM TOLUTANUM (Balsam of Tolu).

A fragrant soft solid balsam obtained from incisions in the trunk of *Myroxylon toluifera* H. B. and K.

USES.

Antiseptic, expectorant.

DISPENSING.

When the tincture is diluted with water, mucilage of acacia is required to suspend the resin.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

PREPARATIONS.

Syrupus Tolutanus.—*Dose*—½ to 2 dr. (2 to 8 mils).
Tinctura Tolutana.—*Dose*—½ to 1 dr. (2 to 4 mils).

BARBITONUM (Barbitone).

SYNONYMS AND PROPRIETARY NAMES.

Barbital, Malonurea, Diethylbarbituric Acid, Diethylmalonyl Urea, Veronal (*Bayer Products, London*).

CHARACTERS.

A white crystalline, odourless powder.

Solubility in water, 1 in 170, 1 in 8½ parts of alcohol. *Soluble* in alkalis and alkaline carbonates.

USES.

Hypnotic.

DISPENSING.

Best administered in cachets, followed by a draught of hot liquid.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

PREPARATION.

Barbitonum Solubile (Soluble Barbitone). — *Synonyms and Proprietary Names*—Barbitalum Solubile, Medinal (*Schering, London*), Veronal Sodium (*Bayer Products, London*). *Characters*—A white crystalline powder. *Soluble* 1 in 6 parts of water. *Dispensing*—Solutions for injection may be prepared by dissolving in the requisite amount of sterilized water, immediately before use. Incompatible with ammonium salts, e.g. the bromides. *Use*—hypnotic. *Dose*—5 to 10 gr. (0·3 to 0·6 gm.).

BARII SULPHAS (Barium Sulphate).

CHARACTERS.

A heavy white amorphous powder, odourless and tasteless. *Insoluble* in water.

USES.

Used for the preparation of barium meals for radiographic work.

PREPARATION.

Pulvis Barii Sulphatis Compositus, B.P.C. (Pulv. Barii Sulphatis Co.).—Compound Powder of Barium Sulphate.

Syn.—Barium Meal; Shadow Meal. Contains 75% of barium sulphate in a cocoa-flavoured powder. *Dose*—4 to 8 ozs. (120 to 240 gm.), mixed immediately before use with sufficient boiling water poured directly on the powder.

BELLADONNÆ FOLIA (Belladonna Leaf).

SYNONYM.

Deadly Nightshade.

Belladonna leaf consists of the dried leaves and tops of *Atropa Belladonna* Linn.

CONSTITUENTS.

Hyoscyamine and possibly atropine; the total quantity of alkaloid being 0·4 to 1·0%, the greater part of which is hyoscyamine.

STORAGE.

Well-closed container in a dry place.

DISPENSING.

When powdered belladonna leaf is prescribed then Belladonna Pulverata (containing 0·3% total alkaloids) must be dispensed.

PREPARATIONS.

Belladonna Pulverata.—Powdered Belladonna Leaf. Is belladonna leaf in fine powder, adjusted with exhausted belladonna leaf to contain 0·3% of alkaloids calculated as hyoscyamine. Anti-spasmodic. Checks excessive secretion, particularly from secretory glands. *Dose*—½ to 3 gr. (0·03 to 0·2 gm.)

Extractum Belladonnæ Siccum.—Dry Extract of Belladonna. 1% of alkaloids. *Uses*—Administered with purgatives to allay griping. *Dose*—¼ to 1 gr. (0·015 to 0·06 gm.).

Tinctura Belladonnæ.—0·03% alkaloids. *Uses*—the tincture is used for the administration of belladonna in mixtures.

Extractum Belladonnæ Viride.—Green Extract of Belladonna. 1% alkaloids. *Uses*—Often prescribed in pill form with purgatives to diminish griping. It is spread on leather or used in the form of Glycerinum Belladonnæ to allay pain or avert glandular secretion, *Dispensing*—When prescribed in a suppository, should be softened with alcohol and water, and

then incorporated with the melted base. *Dose*—¼ to 1 gr. (0·016 to 0·06 gm.).

BELLADONNÆ RADIX (Belladonna Root).

The dried root of *Atropa Belladonna* Linn.

CONSTITUENTS.

Hyoscyamine and possibly atropine. The total alkaloidal content varies from 0·3 to 0·8%.

USES.

Its action resembles that of the leaves, but preparations of the root are chiefly used for external application.

DOSE.

½ to 2 gr. (0·03 to 0·12 gm.).

PREPARATIONS.

Extractum Belladonna Liquidum.—Liquid Extract of Belladonna. 0·75% alkaloids. Used in the preparation of Suppositories of Belladonna. *Dose*—¼ to 1 min. (0·015 to 0·06 mil).

Suppositoria Belladonnæ, B.P. $\frac{1}{60}$ gr. of alkaloids each.

Emplastrum Belladonnæ (10·25%).—These plasters of suitable shape, when applied to the breast, are said to decrease the secretion of milk.

Linimentum Belladonnæ (0·375%).—Used as a local anodyne.

The preparations of belladonna intended for external use, especially the liniment and plaster, may cause fatal poisoning owing to the active principles being absorbed by the skin if applied to too large a surface.

BENZOCAINA (Benzocaine).

SYNONYMS AND PROPRIETARY NAMES.

Ethyl *p*-aminobenzoate, Anæsthesin (*Bayer Products, London*).

CHARACTERS.

A white crystalline powder, odourless, with a slightly bitter taste.

Soluble 1 in 2500 parts of water, 1 in 50 parts of fixed oils.

USES.

Local anæsthetic employed mainly for dusting on mucous or ulcerated surfaces.

DISPENSING.

Administered internally in cachets to relieve pain in gastric carcinoma. Externally applied as a dusting powder, with starch or purified talc, 10 to 50%, or as an ointment with lanolin, 5 to 10%. Solutions of benzocaine in oil are prepared by dissolving the benzocaine in the previously sterilized oil. The final container is then heated to 100° for 30 minutes.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

BENZOINUM (Benzoin).

A balsamic resin obtained from the tree *Styrax Benzoin* Dryand.

CONSTITUENTS.

Contains various esters of benzoic and cinnamic acids together with the free acids.

DOSE.

10 to 30 gr. (0·6 to 2·0 gm.).

PREPARATIONS.

Tinctura Benzoini Simplex, B.P.C. (Tincture of Benzoin).—Diluted with water is used as a stimulant and antiseptic for irritable conditions of the skin. *Dose*—½ to 1 dr. (2 to 4 mils).

Tinctura Benzoini Composita, B.P.C. (Tinct. Benzoin. Co.).—Compound Tincture of Benzoin. *Syn.*—Friar's Balsam. Benzoin, 10 per cent. w/v, storax, balsam of tolu and aloes, macerated in alcohol (90%). *Uses.*—As an antiseptic and styptic for small cuts by applying it undiluted. Internally for chronic gastritis. The vapour from a mixture of tincture and hot water is used as an inhalant. *Dispensing.*—When diluted with water the resin precipitated requires suspending with mucilage of acacia. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

BENZYLIS BENZOAS (Benzyl benzoate).

PROPRIETARY NAME.

Spasmodin (*Bush, London*).

CHARACTERS.

Colourless crystals, or colourless oily liquid. Burning taste. *Soluble* in alcohol, chloroform, and ether. *Insoluble* in water.

USES.

Used externally in the treatment of scabies.

DISPENSING.

Externally used as an emulsion, usually of the following composition: benzyl benzoate, soft soap, industrial methylated equal parts. Proscabin (*Bayer, London*) is a proprietary emulsion of benzyl benzoate.

DOSE.

5 to 8 mins. (0·3 to 0·5 mil) of benzyl benzoate for internal use, in capsules.

BETA-NAPHTHOL (Betanaphthol).

SYNONYM.

Naphthol.

CHARACTERS.

White or nearly white, crystalline lamellæ, or powder. *Soluble* slightly in water, 1 in 2 parts of alcohol (90%), 1 in 12 parts of olive oil. Addition of boric acid increases the solubility in water.

USES.

Intestinal antiseptic, externally as stimulating antiseptic in scaly skin affections.

DISPENSING.

Internally usually in cachets, capsules or tablets. Externally as an ointment, or solution in oil.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

PREPARATIONS.

Unguentum Betanaphtholis Compositum, B.P.C. (Ung. Betanaph. Co.).—Compound Betanaphthol Ointment. *Syn.*—Kaposi's Compound Ointment; Unguentum Naphthol Compositum; Compound Naphthol Ointment. Betanaphthol, about 8·5%, with chalk, soft soap and lard.

BISMUTHI CARBONAS (Bismuth Carbonate).

SYNONYMS.

Bismuth Oxycarbonate, Bismuth Subcarbonate.

CHARACTERS.

A white powder, *insoluble* in water.

USES.

Internally in dyspepsia, gastric inflammation and diarrhœa, forming a protective covering on the walls of the stomach and intestines. Externally in ointments and dusting powder as a sedative and astringent.

DISPENSING.

Best administered in cachets, powders or mixtures. Most varieties are readily diffusible and need no suspending agent. If indiffusible solids are also present use compound powder of tragacanth. Mucilage of acacia produces indiffusible masses in the mixture.

DOSE.

10 to 30 gr. (0·6 to 2·0 gm.).

PREPARATIONS.

Mistura Bismuthi et Sodii Bicarbonatis, B.P.C. (Mist. Bism. et Sod. Bicarb.).—Bismuth and Sodium Bicarbonate Mixture. *Syn.*—Mistura Bismuthi cum Soda; Bismuth and Soda Mixture. Each fluid ounce contains 10 gr. each of bismuth carbonate, sodium bicarbonate and light magnesium carbonate, in distilled water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Pulvis Bismuthi Compositus, B.P.C. (Pulv. Bism. Co.).—Compound Bismuth Powder. Usually supplied for Maclean's Powder. Contains bismuth carbonate 1, calcium carbonate 3, heavy magnesium carbonate 3, sodium bicarbonate 1. *Dose*—¼ to 1 dr. (1 to 4 gm.).

Trochiscus Bismuthi Compositus, B.P.—Compound Lozenge of Bismuth. Contains approximately 2¼ gr. each of bismuth carbonate and heavy magnesium carbonate, and 4½ gr. of calcium carbonate.

Unguentum Bismuthi, B.P.C. (Ung. Bism.).—Bismuth Ointment. Bismuth carbonate, 12·5%, in white soft paraffin.

BISMUTHI SALICYLAS (Bismuth Salicylate).

CHARACTERS.

A white powder, *insoluble* in water and alcohol.

USES.

Intestinal antiseptic and protective. Intramuscularly injected in the treatment of syphilis.

DISPENSING.

Orally in cachets or in mixtures suspended with mucilage of tragacanth. Injected intramuscularly suspended in oil.

DOSE.

10 to 30 gr. (0·6 to 2·0 gm.) orally; 1 to 2 gr. (0·06 to 0·12 gm.) intramuscularly.

PREPARATION.

Injectio Bismuthi Salicylatis, B.P. (10% w/v).—Bismuth salicylate, 10% w/v, with camphor and phenol in sterile olive oil. *Dose*—By intramuscular injection, 10 to 20 min. (0·6 to 1·2 mil).

BISMUTHI SUBGALLAS (Bismuth subgallate).

SYNONYMS AND PROPRIETARY NAMES.

Bismuth oxygallate, Basic bismuth gallate, Dermatol (*Bayer, London*).

CHARACTERS.

A yellow powder, odourless and tasteless.
Insoluble in water, in alcohol and ether.

USES.

Mild astringent. Given orally for diarrhœa. Suppository used for hæmorrhoids. Also used as a dusting powder, alone or mixed with starch, talc or boric acid.

DOSE.

10 to 30 gr. (0·6 to 2·0 gm.).

PREPARATION.

Suppositorium Bismuthi Subgallatis Compositum.—(Compound Bismuth Subgallate Suppository).—Contains Bismuth subgallate, resorcinol, zinc oxide, and Balsam of Peru.

BISMUTHUM PRÆCIPITATUM (Precipitated Bismuth).

CHARACTERS.

A dull grey powder which contains no particles larger than 15 microns in diameter.

USES.

For treatment of syphilis, by intramuscular injection.

DOSE.

1½ to 3 gr. (0·1 to 0·2 gm.) by intramuscular injection.

PREPARATION.

Injectio Bismuthi, B.P. (20%, w/v, Bi.).—*Synonyms and Proprietary Names*—Bisglucol (*May & Baker, London*), Bismostab (*Boots, Nottingham*). Contains 20% of precipitated bismuth with 0·5% v/v of cresol in isotonic dextrose solution. *Dose*—8 to 15 min. (0·5 to 1·0 mil) by intramuscular injection.

BORAX (Borax).

SYNONYMS.

Borax Purificatus, Sodium Borate, Sodium Pyroborate.

CHARACTERS.

Large, transparent, colourless crystals, or white powder. *Soluble* 1 in 25 parts of water, 1 in 1 part of glycerin.

USES.

Mild antiseptic, used as a gargle or lotion.

DISPENSING.

Internally, included in bromide mixtures as a sedative. In mixtures, flavoured with syrup of orange. Externally, in aqueous solution as a lotion. Glycerinum Boracis is used as a throat paint, especially for children.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

PREPARATIONS.

Glycerinum Boracis, B.P. (12% w/w).—Borax 12% w/w, in glycerin. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

Liquor Alkalinus, B.P.C. (Liq. Alk.).—Alkaline Solution. *Syn.*—Collunarium Alkalinum; Alkaline Nasal Wash. Sodium bicarbonate and borax, of each 1·5% w/v, with phenol and sucrose, in distilled water.

Mel Boracis, B.P.—Honey of Borax. 10% of Borax, dissolved in glycerin and honey.

Pulvis Boracis Compositus, B.P.C. (Pulv. Borac. Co.).—Compound Borax Powder. *Syn.*—Pulvis Alkalinus Compositus; Compound Alkaline Powder. Sodium bicarbonate, sodium chloride, borax and sucrose, equal parts.

BROMETHOL (Bromethol).

SYNONYMS AND PROPRIETARY NAMES.

Solution of tribromethyl alcohol, Avertin (*Bayer Products, London*).

CHARACTERS.

A solution of tribromethyl alcohol in amylene hydrate. 1 mil contains 1 gm. of tribromethyl alcohol.

USES.

A basal narcotic, administered by rectal injection.

DISPENSING.

For rectal injection, dilute immediately before use with 39 times its own volume of water at 40° C. Shake well to dissolve. If overheated hydrobromic acid liberated; *p*H tested before use with congo red, colour should be orange; if diluted solution assumes purple or blue colour with indicator, it must be rejected.

DOSE.

$\frac{1}{2}$ to $\frac{2}{3}$ min. per pound of body weight (0·075 to 0·1 mil per kilogram body weight).

BUCHU (Buchu Leaves).

The dried leaves of *Barosma betulina* (Thunb.) Bartland Wendl.

CONSTITUENTS.

Up to 2% of a volatile oil (which contains diosphenol) and mucilage.

USES.

Diuretic and urinary antiseptic.

DISPENSING.

Given preferably as the fresh infusion, often with other diuretics, viz. citrates, acetates, benzoates, hexamine and cubebs.

DOSE.

15 to 30 gr. (1 to 2 gm.).

PREPARATIONS.

Infusum Buchu Recens (5%).—Fresh Infusion of Buchu.

Buchu leaves infused with boiling water for 15 minutes. *Dose*—1 to 2 fl. ozs. (30 to 60 mils).

Infusum Buchu Concentratum.—Concentrated Infusion of Buchu. Prepared by percolating buchu leaves with alcohol (25%). When diluted 1 in 8 yields a preparation approximately equivalent in strength, but not in flavour, to the fresh infusion.

NOTE.—The prescriber must specify Inf. Buchu *Recens* if he wishes the fresh infusion to be dispensed.

CAFFEINA (Caffeine).

SYNONYM.

Theine.

CHARACTERS.

Colourless, silky crystalline needles.

Soluble, 1 in 80 parts of water, 1 in 40 parts of alcohol.

USES.

Cardiac and respiratory stimulant, diuretic. Of value in nervous headache and often given with phenacetin and aspirin.

DISPENSING.

Administered in powders, capsules or tablets.

DOSE.

2 to 5 gr. (0·12 to 0·3 gm.).

PREPARATION

Caffeina et Sodii Benzoas.—Caffeine and Sodium Benzoate. A mixture of equal parts of caffeine and sodium benzoate. A white powder, odourless, bitter taste, completely *soluble* in water, 1 in 4. Action similar to caffeine, employed in hypodermic injection as it is readily soluble. *Dose*—5 to 15 gr. (0·3 to 1·0 gm.) orally. By injection, 2 to 5 gr. (0·12 to 0·3 gm.).

CALCIFEROL (Calciferol).

SYNONYM AND PROPRIETARY NAME.

Vitamin D_2, Radiostol (*British Drug Houses, London*).

CHARACTERS.

Colourless crystals.

Insoluble in water, *soluble* in vegetable oils.

USES.

A preventative and curative for diseases with abnormal calcium and phosphorus metabolism, viz. infantile rickets, osteomalacia, etc.

DOSE.

Prophylactic (daily), for infants, $\frac{1}{2400}$ to $\frac{1}{1200}$ gr. (0·025 to 0·05 mgm.); 1000 to 2000 units. Therapeutic (daily), for infants, $\frac{1}{1200}$ to $\frac{1}{800}$ gr. (0·05 to 0·075 mgm.); 2000 to 3000 units.

PREPARATION.

Liquor Calciferolis, B.P. Add.—A solution of calciferol in fixed oil, containing 3000 units of antirachitic activity per gramme. *Dose*—Prophylactic (daily), for infants, 5 to 10 min. (0·3 to 0·6 mil); 1000 to 2000 units. Therapeutic (daily), for infants, 10 to 15 min. (0·6 to 1·0 mil); 2000 to 3000 units.

CALCII CARBONAS (Calcium Carbonate).

SYNONYM.

Precipitated chalk.

CHARACTERS.

A white, micro-crystalline powder, prepared by interaction between sodium carbonate and calcium chloride.

Insoluble in water.

USES.

Antacid and astringent.

DISPENSING.

Administered in cachets or powders.

DOSE.

15 to 60 gr. (1 to 4 gm.).

PREPARATIONS.

Creta cum Camphora, B.P.C. (Cret. c. Camph.).—Camphorated Chalk. Camphor, 1 in 10, with calcium carbonate.

Pulvis Bismuthi Compositus, B.P.C. (Pulv. Bism. Co.).—Compound Bismuth Powder. Bismuth Carbonate, 1 part; calcium carbonate, 3 parts; heavy magnesium carbonate, 3 parts; sodium bicarbonate, 1 part. *Dose*—$\frac{1}{4}$ to 1 dr. (1 to 4 gm.).

CALCII CHLORIDUM HYDRATUM (Hydrated Calcium Chloride).

CHARACTERS.

Odourless, colourless crystals.
Soluble 4 in 1 part of water.

USES.

Increases the coagulability of the blood. Used for chilblains. Administered in cases of calcium deficiency.

DISPENSING.

When Calcium Chloride is prescribed for injection, twice the prescribed amount of Hydrated Calcium Chloride shall be dispensed. Solutions may be sterilized by heating in an autoclave, or filtration.

STORAGE.

In well-closed containers.

DOSE.

By intramuscular injection, 1 to 3 gr. (0·06 to 0·2 gm.); by intravenous injection, 10 to 30 gr. (0·6 to 2·0 gm.).

CALCII GLUCONAS (Calcium Gluconate).

CHARACTERS.

A white crystalline powder, odourless and tasteless.
Soluble 1 in 30 parts of water.

USES.

For treatment of cases with calcium deficiency.

DISPENSING.

Given orally, or by intramuscular or intravenous injection.

The injection (approximately 10%) is a supersaturated solution, and great care must be taken to clarify this hot solution before filling into well-washed ampoules and sterilizing by autoclaving. If care is not taken solid calcium gluconate will separate.

DOSE.

30 to 60 gr. (2·0 to 4·0 gm.).

PREPARATION.

Injectio Calcii Gluconatis (Injection of Calcium Gluconate). Approximately 10%. *Dose*—150 to 300 mins. (10 to 20 mil).

CALCII HYDROXIDUM (Calcium Hydroxide).

SYNONYM.

Calcii Hydras.

CHARACTERS.

A soft, white powder, with a slightly bitter taste.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

STORAGE.

Should be kept in a well-closed container.

PREPARATION.

Liquor Calcii Hydroxidi.—Solution of Calcium Hydroxide. *Syn.*—Liquor Calcis, Solution of Lime, Lime Water. *Uses*—Externally with zinc oxide and calamine as a skin lotion or liniment; internally administered in milk to infants to prevent the formation of large clots of curd in the stomach. Often prescribed with oils in liniments, where the soap formed by the free fatty acid of the oil, and the lime water serves as the emulgent (w/o emulsions). *Dose*—1 to 4 fl. oz. (30 to 120 mils).

CALCII LACTAS (Calcium Lactate).

CHARACTERS.

A white powder, almost odourless and tasteless.

Solubility varies, about 1 in 18·5 parts of water.

USES.

Useful in urticaria and chilblains. Increases the coagulability of the blood.

DISPENSING.

Sometimes ordered as Calcii Lactas *Recens*, when it should be freshly prepared. The B.P.C. 1934 gives the following directions :—40 gr. of calcium carbonate, with 60 gr. of lactic acid (diluted about 10 times with water, boiled for 20 minutes and filtered) will yield a solution containing about 100 gr. of freshly prepared calcium lactate.

DOSE.

15 to 60 gr. (1 to 4 gm.).

CALUMBA (Calumba).

SYNONYM.

Calumba Radix, Calumba Root.

Calumba is the dried root of *Jateorhiza palmata* (Lamarck) Miers, cut into oblique or transverse slices.

USES.

A simple bitter. Given before meals for its reflex action in dyspepsia associated with hypochlorhydria.

DISPENSING.

Usually dispensed as the infusion or tincture.

DOSE.

10 to 30 gr. (0·6 to 2·0 gm.).

PREPARATIONS.

Infusum Calumbæ Recens.—Calumba root macerated in cold water for 30 minutes. *Dose*—½ fl. oz. (15 to 30 mils).

Infusum Calumbæ Concentratum.—Prepared by triple maceration of calumba with cold water, evaporation and preservation of the product with alcohol. When diluted 1 in 8 parts of distilled water, it yields a preparation approximately equivalent in strength but not in flavour to Inf. Calumba Recens.

NOTE.—The prescriber must specify Inf. Calumba *Recens* on the prescription if he wishes the fresh infusion to be dispensed.

Tinctura Calumbæ.—Prepared by macerating calumba root in alcohol, 60%. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

As calumba root and its preparations do not normally contain tannin, they can, like quassia, be prescribed with all the preparations of iron.

CALX CHLORINATA (Chlorinated Lime).

SYNONYM.

Bleaching Powder, "Chloride of Lime."

CHARACTERS.

Dull white powder, with odour of chlorine.

STORAGE.

Well-closed containers.

PREPARATIONS.

Liquor Sodæ Chlorinatæ Chirurgicalis, B.P.—Surgical Solution of Chlorinated Soda. *Syn.*—Dakin's Solution. Prepared by triturating chlorinated lime with a solution of sodium carbonate, shaking, filtering and dissolving boric acid in the solution. A non-irritant antiseptic for wounds. Fresh quantities should be brought in contact frequently.

Liquor Calcis Chlorinatæ cum Acido Borico, B.P.C.—(Liq. Calc. Chlorinat. c. Acid. Boric.).—Solution of Chlorinated Lime with Boric Acid. *Syn.*—Eusol. It contains, when freshly prepared, about 0·4% of available chlorine. An antiseptic solution.

"Bleach Cream."—A paste of "tropical bleaching powder" 3, water 5, by weight. For decontamination of mustard gas. "Tropical bleach" is bleaching powder with excess of lime.

"Bleach Ointment."—Anti-gas Ointment No. 1. Rubbed in well within 3 mins. of exposure to mustard gas contamination and wiped off after one minute. Equal parts of bleaching powder and white soft paraffin.

CAMPHORA (Camphor).

CHARACTERS.

A white crystalline substance obtained from *Cinnamomum Camphora* Nees and Eberm., and purified by sublimation; or it may be obtained synthetically from the pinene of oil of turpentine.

Soluble 1 in 700 parts of water, very soluble in alcohol, ether, chloroform and fixed oils.

USES.

Externally as a mild counter irritant and rubifacient. Internally (orally) as a carminative in flatulence. It is injected hypodermically as Injectio Camphoræ or Injectio Camphoræ Ætheræ, as a restorative in collapse.

DISPENSING.

For internal use camphor is administered as Spirit of Camphor or in pills. Also as essence of camphor (an alcoholic solution 1 in 2½) given on sugar or in milk.

For injection the camphor should be dissolved in the filtered oil and the solution heated in ampoules to 150° for one hour.

When the ethereal solution has to be dispensed the camphor in oil should be treated similarly in bulk, or in ampoules, the solution cooled and the ether incorporated with aseptic technique. Heating in the final containers at 100° for half an hour is prescribed in the B.P.C.

DOSE.

Orally 2 to 5 gr. (0·12 to 0·3 gm.). Subcutaneous injection 1 to 3 gr. (0·06 to 0·2 gm.).

PREPARATIONS.

Aqua Camphoræ, B.P.—½ gr. in 1 oz. Prepared by dissolving camphor in alcohol (90%) and adding gradually to water. A vehicle for more active remedies.

Creta cum Camphora, B.P.C. (Cret. c. Camph.).—Camphorated chalk. Camphor, 1 in 10, with calcium carbonate.

Injectio Camphoræ, B.P.C. (Inj. Camph.).—Injection of Camphor. Camphor, 1 in 10, in olive oil. *Dose*—8 to 30 min. (0·5 to 2 mils) by subcutaneous injection.

Injectio Camphoræ Æthereæ, B.P.C. (Inj. Camph. Æther.).—Ethereal Injection of Camphor. *Syn.*—Curschmann's Solution. Camphor, 1 in 5, and ether, about 1 in 3, in olive oil. *Dose*—4 to 15 m. (0·25 to 1 mil), by subcutaneous injection.

Linctus Camphoræ Compositus, B.P.C. (Linct. Camph. Co.).—Compound Linctus of Camphor. Camphorated tincture of opium, 1 in 4, with emulsion of chloroform, syrup of wild cherry, oxymel of squill, solution of bordeaux B and concentrated infusion of senega. *Dose.*—½ to 2 dr. (2 to 8 mils).

Linimentum Camphoræ, B.P.—*Syn.*—Camphorated Oil. Camphor, 20%, in olive oil.

Linimentum Camphoræ Ammoniatum, B.P.—*Syn.*—Compound Liniment of Camphor. Camphor, 12·5% w/v, strong solution of ammonia, 25% v/v, in alcohol, perfumed with oil of lavender.

Spiritus Camphoræ, B.P.—Camphor, 10% w/v, in alcohol (90%). *Dose*—5 to 30 min. (0·3 to 2 mils).

Tinctura Opii Camphorata, B.P.—*Syn.*—Paregoric, Tinct. Camph. Co., Compound Tincture of Camphor. Tincture of Opium, 5% v/v, with camphor, benzoic acid, oil of anise and alcohol. Contains 0·05% of anhydrous morphine or $\frac{1}{37}$ gr. of morphine in each fluid drachm. Sedative in cough. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

CANTHARIDINUM (Cantharidin).

CHARACTERS.

Colourless, odourless, crystals. Obtained from various species of Cantharis or Mylabris.

USES.

Vesicant and counter irritant.

CAUTION.—Use with great care.

PREPARATIONS.

Emplastrum Cantharidini (0·2% w/w).—*Syn.*—Cantharidin Plaster, Blistering Plaster. Cantharidin in acetone, with yellow beeswax, wool fat, and castor oil. Vesicant; generally blisters in from 6 to 9 hours.

Liquor Epispasticus.—Blistering Liquid. 0·4% w/w. Cantharidin, castor oil, and colophony in acetone.

CAPSICUM (Capsicum).

SYNONYMS.

Capsici Fructus, Capsicum Fruit.

The dried ripe fruits of *Capsicum minimum* Roxb. Known as Cayenne Pepper.

Active principle—Capsaicin.

USES.

Internally as a powerful stimulant and carminative to the alimentary canal.

Externally as an irritant, producing warmth, redness and vesication.

DISPENSING.

Internally as the tincture, or, to cover its pungent taste, in pills.

Externally the strong tinctura (Tinctura Capsici Fortior), liniment, and ointment are used.

DOSE.

½ to 2 gr. (0·03 to 0·12 gm.).

PREPARATIONS.

Gossypium Capsici, B.P.C. (Gossyp. Capsic.).—Capsicum wool contains the equivalent of 20% of capsicum.

Linimentum Capsici, B.P.C. (Lin. Capsic.).—Liniment of Capsicum. Strong tincture of capsicum, 1 in 3, with oleic acid, oil of lavender and alcohol (90%).

Tinctura Capsici, B.P.—Tincture of Capsicum. Prepared by maceration with 60% alcohol. *Dose*—5 to 15 min. (0·3 to 1·0 mil).

Tinctura Capsici Fortior, B.P.C. (Tinct. Capsic. Fort.).—Stronger Tincture of Capsicum. *Syn.*—Turnbull's Tincture of Capsicum. 1 in 3. *Dose*—1 to 3 min. (0·06 to 0·2 mil).

Unguentum Capsici, B.P.—Capsicum Ointment. The active principles of capsicum extracted by digestion, with lard, and hard and soft paraffins.

Unguentum Capsici Compositum, B.P.C. (Ung. Capsici Co.).—Compound Capsicum Ointment. *Syn.*—Compound Capsicum Oleoresin Ointment, Chillie Paste. Oleoresin of capsicum, 2%, with menthol, chloral hydrate, and camphor, in yellow soft paraffin.

CARBACHOLUM (Carbachol).

SYNONYMS AND PROPRIETARY NAMES.

Carbamylcholine chloride, Moryl (*Savory & Moore, London*), Choryl (*Pharmaceutical Products, London*), formerly sold as Doryl.

CHARACTERS.

Small colourless crystals; very hygroscopic.

Soluble—very *soluble* in water, very slightly *soluble* in cold dehydrated alcohol, more *soluble* in hot alcohol. *Insoluble* in acetone and ether.

USES.

Exerts a similar effect to acetylcholine, but is active orally. Used to relieve post-operative intestinal atony, and retention of urine.

DISPENSING.

Solutions can be sterilized by autoclaving or filtration. Administered subcutaneously, intramuscularly or by mouth.

DOSE.

$\frac{1}{64}$ to $\frac{1}{16}$ gr. (0·001 to 0·004 gm.). Subcutaneous injection—$\frac{1}{240}$ to $\frac{1}{120}$ gr. (0·00025 to 0·0005 gm.).

CARBROMALUM (Carbromal).

SYNONYMS AND PROPRIETARY NAMES.

Uradil, α-Bromo-α-ethylbutyryl carbamide, Adalin (*Bayer Products, London*), Nyctal (*Sitsa, Paris ; Roberts, London*), Planadalin (*May & Baker, London*).

CHARACTERS.

A white crystalline powder, almost odourless and tasteless. Sparingly *soluble* in water.

USES.

Hypnotic.

DISPENSING.

Commonly given in tablets or cachets, followed by a hot drink, 30 minutes before bedtime.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

CARDAMOMUM (Cardamom).

The dried ripe or nearly ripe seeds of *Eletteria Cardamomum Maton*, var. *minuscula Burkhill*. Kept in their pericarps until required.

USES.

Carminative and antispasmodic.

DOSE.

10 to 30 gr. (0·6 to 2 gm.).

PREPARATION.

Tinctura Cardamomi Composita.—Cardamom, caraway, and cochineal are percolated with alcohol (60%) and glycerin added. Carminative. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

CARYOPHYLLUM (Clove).

The dried flower buds of *Eugenia aromatica* (Linn.) Baill.

USES.

Stimulant and carminative to the alimentary canal. The infusion and water are useful adjuvants for alkalis and aromatics.

DOSE.

2 to 5 gr. (0·12 to 0·3 gm.).

PREPARATIONS.

Infusum Caryophylli Recens.—Prepared by infusing bruised clove in boiling water for 15 minutes. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Infusum Caryophylli Concentratum.—Prepared by Maceration of bruised clove in alcohol 25%. When diluted 1 in 8 with distilled water it yields a preparation approximately equivalent in strength but not in flavour to Infusum Caryophylli Recens.

NOTE.—The prescriber must specify Inf. Caryoph. *Recens* if he wishes fresh infusion to be dispensed.

CASCARA SAGRADA (Cascara Sagrada).

The dried bark of *Rhamnus purshiana*, D.C.

USES.

Mild laxative acting principally on the large intestine.

DOSE.

20 to 60 gr. (1·4 to 4·0 gm.).

PREPARATIONS.

Elixir Cascaræ Sagradæ, B.P.—Elixir of Cascara Sagrada. An aqueous extract of cascara sagrada, 1 in 1, made less bitter with magnesium oxide, and flavoured with liquorice, soluble saccharin, oil of coriander, oil of anise, alcohol and glycerin. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

Extractum Cascaræ Sagradæ Siccum, B.P.—Extract of Cascara Sagrada. An aqueous percolate from cascara, evaporated under reduced pressure, and granulated. *Dose*—2 to 8 gr. (0·12 to 0·5 gm.).

Mistura Cascaræ Composita, B.P.C. (Mist. Casc. Co.).—Compound Mixture of Cascara. Each fluid ounce contains 20 min. of liquid extract of cascara, 5 min. each of tinctures of belladonna and nux vomica, with liquid extract of liquorice, aromatic spirit of ammonia, glycerin and chloroform water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Pilulæ Cascaræ Compositæ, B.P.C. (Pil. Casc. Co.).—Compound Cascara Pills. *Syn.*—Cascaræ, Belladonnæ et Nucis Vomicæ. Each pill contains ⅘ gr. dry extract of cascara, and $\frac{1}{10}$ gr. each of the dry extracts of belladonna and nux vomica.

CATECHU (Catechu).

A dried aqueous extract from the leaves and young shoots of *Uncaria gambier* (Hunter) Roxb.

USES.

A powerful astringent. It is used internally with other astringents as Pulvis Catechu Compositus and as Tinctura Catechu in diarrhœa and hæmorrhage from the alimentary canal.

DOSE.

5 to 15 gr. (0·3 to 1 gm.).

PREPARATIONS.

Pulvis Catechu Compositus, B.P.C. (Pulv. Catech. Co.). Compound Powder of Catechu. Catechu, 1 in 2½, with kino, krameria, cinnamon and nutmeg. *Dose*—10 to 60 gr. (0·6 to 4 gm.).

Tinctura Catechu, B.P.—Tincture of Catechu. Prepared by macerating catechu and cinnamon with 45 per cent. alcohol. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

CHINIOFONUM (Chiniofon).

SYNONYMS AND PROPRIETARY NAMES.

Pulvis Chiniofoni, Loretin (*Schuchardt, Gorlitz*), Quinoxyl (*Burroughs Wellcome, London*), Yatren (*Bayer Products, London*).

CHARACTERS.

A light yellow powder, odourless, with taste at first bitter, then sweet.

Soluble with effervescence in about 25 parts of water.

USES.

Amœbic dysentery.

DOSE.

1 to 8 gr. (0·06 to 0·5 gm.); by rectal injection, 15 to 75 gr. (1 to 5 gm.).

CHLORALIS HYDRAS (Chloral Hydrate).

CHARACTERS.

Colourless, transparent, crystals, with a pungent odour and taste.

Soluble 4 parts in 1 of water.

USES.

Hypnotic and sedative.

DISPENSING.

Usually administered in dilute solution as syrup of chloral or with bromides. Should not be taken as tablets or pills.

DOSE.

5 to 20 gr. (0·3 to 1·2 gm.).

PREPARATIONS.

Liquor Bromidi Compositus, B.P.C. (Liq. Brom. Co.).—Compound Bromide Solution. *Syn.*—Liquor Bromochloral Compositus. Each fluid drachm contains 15 gr. of chloral hydrate, 15 gr. of potassium bromide, with extract of cannabis, liquid extract of hyoscyamus, tincture of orange, and glycerin. *Dose*—½ to 2 fl. dr. (2 to 8 mils).

Syrupus Chloralis, B.P.C. (Syr. Chloral.).—Syrup of Chloral. Chloral hydrate, 1 in 5, in distilled water and syrup; each fluid drachm contains about 11 gr. of chloral hydrate. *Dose*—½ to 2 fl. dr. (2 to 8 mils).

CHLORAMINA (Chloramine).

SYNONYMS AND PROPRIETARY NAMES.

Chloramine T, Mianin, Chlorazene (*Abbott, Montreal; Pharmaceutical Products, London*), Tolamine (*Burroughs Wellcome, London*), *p*-Toluene sodium sulphochloramide.

CHARACTERS.

White crystals or crystalline powder, with a faint odour of chlorine and an unpleasant taste.

Soluble 1 in 7 parts of water, 1 in 12 parts of alcohol (90%).

USES.

A powerful antiseptic; sometimes used instead of hypochlorites for irrigation of wounds.

DISPENSING.

Use a 2% solution for irrigation, and a 0·5% solution as a mouthwash.

PREPARATION.

Anti-gas ointment No. 2.—Chloramine in vanishing cream, Used for mustard gas and lewisite contamination.

CHLORBUTOL (Chlorbutol).

CHARACTERS.

Colourless, volatile, crystals with a camphoraceous odour.

Soluble 1 part in 125 of water, 1 part in 1 of alcohol (90%), and 1 part in 10 of glycerin.

USES.

Sedative, analgesic and antiseptic.

DISPENSING.

May be administered in powders, which should be dispensed preferably in a bottle, if they are to be kept. Best administered in gelatin capsules.

DOSE.

5 to 20 gr. (0·3 to 1·2 gm.).

CHLOROCRESOL (Chlorocresol).

SYNONYM.

Para-chlor-meta-cresol.

CHARACTERS.

White crystals, characteristic odour.

Soluble in 250 parts of water. More *soluble* in hot water. *Soluble* in alcohol, ether, fixed oils and in solution of sodium hydroxide.

USES.

More powerful bactericide than phenol and has a relatively low toxicity. A 0·05% solution has been shown to be about 1·5 times as active as 0·5% phenol against an aerial micrococcus; the two solutions have approximately equal activity against Bact. coli. An 0·1% solution has been recommended as a bacteriostatic in parenteral injections. It is certainly more active in this concentration than 0·5% phenol.

Aqueous solutions may be sterilized (if stable) by incorporating 0·2% and steaming at 98° C. for half an hour.

Rideal-Walker Coefficient given as 14·0 to 40·0. Lower figure probably more accurate.

CHLOROFORMUM (Chloroform).

CHARACTERS.

A colourless, volatile liquid. Not inflammable. S.G. 1·485 to 1·490.

Soluble 1 part in 200 of water. *Miscible* with fixed and volatile oils, ether, dehydrated alcohol and most organic solvents.

STORAGE.

In well-closed containers, glass-stoppered bottles, protected from the light.

USES.

General anæsthetic when inhaled. Carminative when swallowed. Externally rubefacient and anodyne.

DOSE.

1 to 5 min. (0·06 to 0·3 mil).

PREPARATIONS.

Aqua Chloroformi (0·25%).—Used as a vehicle. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Spiritus Chloroformi (Spirit of Chloroform).—5%. *Syn.*—Chloric Ether, Spirit of Chloric Ether. Chloroform, 1 in 90% of alcohol to make 20. *Dose*—5 to 30 min. (0·3 to 2·0 mils).

CHLOROXYLENOL (Chloroxylenol).

SYNONYM.

Para-chlor-meta-xylenol.

CHARACTERS.

A white crystalline solid. Slightly *soluble* in water—about 3 in 10,000. More *soluble* in alkalis.

USES.

A powerful bactericide, but its low solubility limits its use in aqueous solution. More soluble in soap solutions, and often used in triethanolamine soap mixture. "Dettol" is stated to be a solution of a halogen derivative of xylenol, in certain essential oils.

PREPARATION.

Liquor Antisepticus, N.F.—Is a solution of chloroxylenol in a triethanolamine ricinoleate, with ti-tree oil.

Liquor Chloroxylenolis (Solution of Chlorxylenol) *Synonym*—Surgical Antiseptic Solution is a 5% solution of Chlorxylenol in a sodium ricinoleate soap solution, with alcohol and terpineol.

CHRYSAROBINUM (Chrysarobin).

CHARACTERS.

A crystalline yellow powder, obtained from Araroba, a substance found in the cavities in the trunk of *Andira Araroba* by extracting with hot benzene, evaporating to dryness and powdering.

USES.

Antiparasitic in skin diseases, viz. psoriasis and ringworm of the scalp and glabrous skin.

DISPENSING.

As an ointment or pigment. Should not be applied over a large area of the skin. The pigment does not stain linen.

PREPARATIONS.

Pigmentum Chrysarobini, B.P.C. (Pig. Chrysarob.).—Chrysarobin Paint. Chrysarobin, 1 in 10 in solution of gutta percha.

Unguentum Chrysarobini, B.P.—Chrysarobin Ointment. Chrysarobin 4% in simple ointment.

CINCHONA (Cinchona).

SYNONYMS

Cinchonæ Rubræ Cortex, Red Cinchona Bark, Jesuit's Bark, Peruvian Bark.

The dried bark of cultivated trees of *Cinchona calisaya* Weddell, *Cinchona ledgeriana* Moens, *Cinchona officinalis* Linn., *Cinchona Succirubra* and hybrids of the last two species with either of the first two. It should contain not less than 6% of total alkaloids, of which not less than half should be quinine and cinchonidine.

USES.

Bitter tonic. Antipyretic.

DISPENSING.

Generally prescribed as the liquid extract or tincture. If

dispensed with ammonium carbonate requires mucilage of acacia to suspend the precipitated alkaloids.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

PREPARATIONS.

Extractum Cinchonæ Liquidum (5% alkaloids).—Prepared by mixing extract of cinchona with alcohol (90%), glycerin, hydrochloric acid, and adjusting with distilled water. *Dose*—5 to 15 min. (0·3 to 1·0 mil).

Tinctura Cinchonæ, B.P. (1% w/v.)—Prepared by mixing extract of cinchona with alcohol. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

Tincture Cinchonæ Composita, B.P. (0·5% w/v).—Extract of cinchona dissolved in the liquid obtained by macerating dried bitter orange peel, serpentary rhizome, and cochineal in alcohol (70%). *Use*—Prophylactic for the common cold. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

CINCHOPHENUM (Cinchophen).

SYNONYMS AND PROPRIETARY NAMES.

Acidum Phenylcinchoninicum, Quinophan, 2-Phenylquinoline-4-Carboxylic Acid, Agotan (*Howard & Sons, Ilford*), Actocin (*Cavendish Chemical Co., London*), Atophan (*Schering, London*), Phenoquin (*Southall Bros. & Barclay, Birmingham*), Tophosan (*Richter, London*).

CHARACTERS.

A white or yellowish powder or crystals, odourless, with a slightly bitter taste.

Insoluble in water, *soluble* 1 in 120 parts of alcohol (95%), and in solutions of alkali hydroxides, carbonates, and bicarbonates.

USES.

Increases the excretion of uric acid. (CAUTION.—Keep the patient under constant observation; cinchophen sometimes causes acute yellow atrophy of the liver.)

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

CINNAMOMUM (Cinnamon).

The dried inner bark of the shoots of coppiced trees of *Cinnamomum zeylanicum* Nees.

USES.

Carminative and slightly astringent. Aqua Cinnamomi is a useful aromatic vehicle. Pulvis Cinnamomi Compositus, B.P.C., is employed as an intestinal astringent and stimulant in diarrhœa.

DOSE.

5 to 20 gr. (0·3 to 1·2 gm.).

PREPARATIONS.

Aqua Cinnamomi Destillata, B.P.—A colourless water obtained by distilling bruised cinnamon bark and water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Aqua Cinnamomi Concentratum.—Prepared by dissolving oil of cinnamon in alcohol (90%) and gradually adding water. Talc is then added and the solution filtered. When diluted 1 in 40 with distilled water, it yields a preparation which is approximately equivalent in strength to Aqua Cinnam. Dest., but contains a little alcohol.

NOTE.—The prescriber must specify Aq. Cinnam. Dest., if he desires Distilled Cinnamon Water to be dispensed.

Pulvis Cinnamomi Compositus, B.P.C.—*Syn.*—Pulvis Aromaticus. Equal parts of cinnamon, cardamom and ginger. *Dose*—10 to 60 gr. (0·6 to 4 gm.).

COCAINA (Cocaine).

CHARACTERS.

Colourless crystals, odourless, bitter taste followed by a sensation of tingling and numbness.

Insoluble in water, *soluble* 1 in 10 parts of alcohol (90%), 1 in 10 parts of castor oil, and 1 in 24 parts of olive oil.

USES.

Powerful local anæsthetic. The base is used for the preparation of oily solutions and ointments.

DOSE.

⅛ to ¼ gr. (0·008 to 0·016 gm.).

PREPARATIONS.

Cocainæ Hydrochloridum.—Colourless, transparent crystals, odourless, bitter taste, followed by a sensation of tingling and numbness. *Soluble* 2 in 1 part of water, 1 in 3 parts of alcohol, and 1 in 3 parts of glycerin. Solutions for injection may be sterilized by heating with a bactericide or filtration. All glass containers must be alkali-free. Powerful local anæsthetic. *Dose*—$\frac{1}{8}$ to $\frac{1}{4}$ gr. (0·008 to 0·016 gm.).

Oculentum Cocainæ, B.P. (Cocaine Eye Ointment).—0·25%.

Trochiscus Krameria et Cocainæ, B.P.—*Syn.*—Krameria and Cocaine Lozenge. Each lozenge contains 1 gr. of dry extract of krameria, and $\frac{1}{20}$ gr. of cocaine hydrochloride.

COCCUS (Cochineal).

The wrinkled oval dried female insect, *Dactylopius coccus* Costa, containing eggs and larvæ.

USES.

Rich red, harmless, colouring agent.

PREPARATIONS.

Liquor Cocci, B.P.C.—*Syn.*—Liquid Cochineal. Cochineal 10%, with potassium carbonate, potassium citrate, alcohol (90%) and distilled water.

Liquor Rosæ Dulcis, B.P.C. (Sweet Solution of Rose).—Cochineal, 1 in 25, with oil of rose, potassium carbonate, potassium acid tartrate, potash alum, glycerin, alcohol (90%) and distilled water.

Tinctura Cocci, B.P.—Cochineal macerated with 45% alcohol. *Dose*—5 to 15 min. (0·3 to 1·0 mil).

CODEINA (Codeine).

CHARACTERS.

Colourless, translucent, odourless crystals, with a bitter taste.

Soluble 1 in 120 parts of water, 1 in 2 parts of alcohol (90%).

USES.

A mild hypnotic. Much used as a sedative in cough.

DOSE.

$\frac{1}{4}$ to 1 gr. (0·016 to 0·06 gm.).

PREPARATIONS.

Codeinæ Phosphas (Codeine Phosphate).—Colourless, odourless, crystals, or powder, with a bitter taste. *Soluble* 1 in 3·5 parts of water. *Dose*—$\frac{1}{4}$ to 1 gr. (0·016 to 0·06 gm.).

Linctus Codeinæ, B.P.C.—Each fluid drachm contains codeine phosphate, $\frac{1}{8}$ gr., with citric acid, emulsion of chloroform, glycerin and mucilage of tragacanth. *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

Syrupus Codeinæ Phosphatis, B.P.C.—Each fluid drachm contains about $\frac{1}{4}$ gr. of codeine phosphate. *Dose*—$\frac{1}{2}$ to 2 fl. dr. (2 to 8 mils).

COLCHICI CORMUS (Colchicum Corm).

The fresh corm of *Colchicum autumnale* Linn., and the same stripped of its coats, sliced transversely and dried at a temperature not exceeding 65° C. It should contain not less than 0·25 per cent. of colchicine.

USES.

Relieves the pain and inflammation of acute gout.

DISPENSING.

The powdered dried corm may be dispensed in pills, or the drug may be dispensed as Vinum Colchici or Extractum Colchici Siccum. The use of hyoscyamus or belladonna with colchicum removes any intestinal irritation.

DOSE.

Of the dried corm, 2 to 5 gr. (0·12 to 0·3 gm.).

PREPARATIONS.

Extractum Colchici Siccum, B.P.—1% Colchicine. Prepared by exhausting the dried corm with 60% alcohol, evaporating under reduced pressure, assaying and adjusting with lactose. *Dose*—$\frac{1}{4}$ to 1 gr. (0·016 to 0·06 gm.).

Pilulæ Colchici et Aloes, B.P.C.—Each pill contains $\frac{1}{4}$ gr. of dry extract of colchicum, dry extract of hyoscyamus and aloes. *Dose*—1 to 4 pills.

Vinum Colchici, B.P.C.—Colchicum corm macerated in sherry type wine. *Dose*—10 to 30 min. (0·6 to 2 mils).

COLCHICI SEMEN (Colchici Semen).

The dried ripe seeds of *Colchicum autumnale* Linn., containing not less than 0·3% of Colchicine.

USES.
As for the corm.

DOSE.
2 to 5 gr. (0·12 to 0·3 gm.).

PREPARATIONS.
Extractum Colchici Liquidum, B.P. (0·3% w/v colchicine).—Prepared by percolation of defatted colchicum seeds, with 60% alcohol and subsequent assaying and adjustment to volume. *Dose*—2 to 5 min. (0·12 to 0·3 mil).

Tinctura Colchici, B.P. (0·03% w/v Colchicine).—Prepared by diluting the liquid extract with alcohol 60%. *Dose*—5 to 15 min. (0·3 to 1·0 mil).

COLLODION FLEXILE (Flexile Collodion).

SYNONYM.
Collodion.

CHARACTERS.
A very viscous solution of pyroxylin, colophony and castor oil in a mixture of alcohol (90%) and ether. The colour varies from a light yellow to dark brown, depending upon the colour of the colophony used.

USES.
For painting on abrasions. It leaves a flexible protective film on drying.

COLOCYNTHIS (Colocynth).

SYNONYMS.
Colocynthidis Pulpa, Colocynth Pulp, Bitter Apple.
The dried pulp of the fruit of *Citrullus Colocynthis* Schrad., the seeds being rejected.

USES.
A powerful hydragogue cathartic. Rarely used alone, on account of its drastic nature, but an important ingredient in many purgative preparations.

DOSE.

2 to 5 gr. (0·12 to 0·3 gm.).

PREPARATIONS.

Extractum Colocynthidis Compositum, B.P.—Contains aloes, scammony resin, curd soap, and cardamom, mixed with an extract prepared from colocynth by maceration with alcohol (60%) and evaporation. *Dose*—2 to 8 gr. (0·12 to 0·5 gm.).

Pilulæ Colocynthidis et Hyoscyami, B.P.—Contains colocynth, aloes, scammony resin, curd soap, dry extract of hyoscyamus. *Dose*—4 to 8 gr. (0·25 to 0·5 gm.).

COPAIBA (Copaiba).

A yellow to yellow-brown viscous oleoresin obtained from the trunk of various species of *Copaifera*.

USES.

Stimulant and antiseptic to urinary and bronchial mucous surfaces.

DISPENSING.

Often dispensed in gelatin capsules. When dispensed in mixtures with solution of potassium hydroxide a resin soap is formed which serves as an emulgent. If prescribed in mixtures without an alkali, powdered gum acacia (an equal quantity) suffices to make an emulsion.

DOSE.

10 to 30 min. (0·6 to 2 mils).

PREPARATIONS.

Liquor Copaibæ, B.P.C.—*Syn.*—Soluble Copaiba. Copaiba, 1 in 2, in solution of potassium hydroxide. *Dose*—1 to 2 fl. dr. (4 to 8 mils).

Liquor Copaiba, Buchu et Cubebæ, B.P.C.—Solution of Copaiba (B.P.C.), 4 in 5, with liquid extracts of buchu and cubebs. *Dose*—1 to 2 fl. dr. (4 to 8 mils).

CREOSOTUM (Creosote).

CHARACTERS.

A colourless or pale yellow oily liquid, with a strong some-

what tarry odour, a product of the distillation of beech tar. It consists of a mixture of guaiacol, cresol and other phenols.

USES.

A powerful antiseptic and deodorant.

DISPENSING.

Internally administered as Syrupus Creosoti Compositus, or in solution in water flavoured with Spirit of Juniper and Liquid Extract of Liquorice. Also in capsules, when it should be diluted with oil.

DOSE.

2 to 10 min. (0·12 to 0·6 mil).

PREPARATION.

Syrupus Creosoti Compositus, B.P.C.—Each fluid drachm contains one minim of creosote with spirit of chloroform, glycerin, syrup of pine and syrup. *Dose*—1 to 2 fl. dr. (4 to 8 mils).

CRESOL (Cresol).

Cresol is a mixture of cresols, xylenols and other homologues obtained from coal tar.

CHARACTERS.

An almost colourless or pale brown liquid with characteristic odour.

Soluble about 1 in 50 parts of water. *Miscible* with alcohol.

USES.

Antiseptic.

DOSE.

1 to 3 min. (0·06 to 0·2 mil).

PREPARATION.

Liquor Cresol Saponatus, B.P.—Solution of Cresol with Soap). *Syn.*—Lysol. A 50% solution of cresol in a saponaceous solvent. It may be prepared by dissolving cresol in linseed oil saponified with potassium hydroxide. A 5% solution in water should be clear and show no opalescence on standing.

CRETA (Chalk).

CHARACTERS.

Native Calcium Carbonate in white friable masses or white powder, freed from its impurities by elutriation.

USES.

Antacid and astringent. For diarrhœa it is administered as Mistura Creta, Mistura Cretæ Composita, or with aromatics in the form of Pulvis Cretæ Aromaticus with or without opium.

DOSE.

15 to 60 gr. (1 to 4 gm.).

PREPARATIONS.

Mistura Cretæ, B.P.C.—Each fluid ounce contains about 13 gr. of chalk, with sucrose, tragacanth, and cinnamon water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Mistura Cretæ Composita, B.P.C.—Each fluid ounce contains 9 gr. of aromatic powder of chalk, 9 gr. of chalk, 30 min. of tincture of catechu, and 3 min. of tincture of opium with sucrose, aromatic spirits of ammonia, compound tincture of cardamom, tragacanth and cinnamon water. *Dose*—1 fl. oz. (30 mils) for an adult ; ½ fl. oz. (15 mils) for a child 12 years old ; 2 fl. dr. (8 mils) for a child 7 years old.

Pulvis Cretæ Aromaticus, B.P.—Chalk 25% with cinnamon, nutmeg, clove, cardamom and sucrose. *Dose*—10 to 60 gr. (0·6 to 4·0 gm.).

Pulvis Cretæ Aromaticus cum Opio, B.P.—Powdered Opium 2·5%, with aromatic powder of chalk. *Dose*—10 to 60 gr. (0·6 to 4·0 gm.).

DESOXYCORTICOSTERONUM ACETAS (Desoxycorticosterone Acetate).

PROPRIETARY NAMES.

D.O.C.A. (*Organon Laboratories, London*), Percorten (*Ciba, Horsham*), Syncortyl (*Roussel Laboratories, London*).

CHARACTERS.

A crystalline compound, *soluble* in oil.

USES.

For the treatment of Addison's disease.

DISPENSING.

Usually administered as oily solution by intramuscular injection. Tablets containing about 100 mg. have been inserted under the skin, and serve as a substitution therapy for those patients who have been restored to some degree of health by injection.

DOSE.

$\frac{1}{30}$th to $\frac{1}{4}$ gr. (2 to 15 mgm.).

DEXTROSUM (Dextrose).

SYNONYMS AND PROPRIETARY NAMES.

Medicinal Glucose (Anhydrous), Grape Sugar, Dextrosol (*Corn Products, London*).

CHARACTERS.

A white crystalline or granular powder with a sweet taste. *Soluble* more than 1 in 1 part of water.

USES.

Administered either orally or parenterally in conditions involving a carbohydrate deficiency.

DISPENSING.

Solutions for injection can be sterilized by autoclaving, or filtration. A 5% solution is approximately isotonic with blood serum.

PREPARATION.

Liquor Dextrosi et Sodii Chloridi, B.P.C. (Liq. Dextros et Sod. Chlor.).—Dextrose and Sodium Chloride Solution. *Syn.*—Glucose-saline Solution. A sterile aqueous solution containing 5% w/v of dextrose and 0·9% w/v of sodium chloride.

DIAMORPHINÆ HYDROCHLORIDUM (Diamorphine Hydrochloride).

SYNONYMS AND PROPRIETARY NAME.

Diacetylmorphine Hydrochloride, Heroin Hydrochloride (*Bayer Products, London*).

CHARACTERS.

A colourless, odourless, crystalline powder.

Soluble 1 in 2 parts of water, 1 in 11 parts of alcohol (90%).

USES.

Hypnotic, analgesic. Sedative for cough.

DISPENSING.

For cough it may be administered as elixir, linctus or pastille. Solutions for injection may be sterilized by heating with a bactericide or filtration, and all glass containers must comply with the tests for limit of alkalinity.

DOSE.

$\frac{1}{25}$ to $\frac{1}{8}$ gr. (0·0025 to 0·008 gm.).

PREPARATIONS.

Elixir Diamorphinæ et Pini Compositum, B.P.C. (Elix. Diamorph. et Pini Co.).—Compound Elixir of Diamorphine and Pine. Each fluid drachm contains approximately $\frac{1}{15}$ gr. of diamorphine hydrochloride and $\frac{5}{16}$ gr. of terpin hydrate, with oil of pumilio pine, alcohol (90%), glycerin and sucrose, coloured with compound solution of tartrazine. *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

Elixir Diamorphinæ et Terpini, B.P.C. (Elix. Diamorph. et Terpin.).—Elixir of Diamorphine and Terpin. Each fluid drachm contains approximately $\frac{1}{18}$ gr. of diamorphine hydrochloride and $\frac{5}{18}$ gr. of terpin hydrate, with alcohol (90%), glycerin and syrup of wild cherry. *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

Linctus Diamorphinæ Camphoratus, B.P.C. (Linct. Diamorph. Camph.).—Camphorated Linctus of Diamorphine. Each fluid drachm contains $\frac{1}{40}$ gr. of diamorphine hydrochloride and $\frac{3}{4}$ min. of liquid extract of ipecacuanha, with camphor, benzoic acid, oil of anise, tincture of squill and syrup. *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

Linctus Diamorphinæ et Scillæ, B.P.C. (Linct. Diamorph. et Scill.).—Linctus of Diamorphine and Squill. Each fluid drachm contains $\frac{1}{40}$ gr. of diamorphine hydrochloride and $\frac{1}{20}$ gr. of sodium antimonyltartrate with liquid extracts of senega and squill, glycerin and syrup. *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

Pastilli Diamorphinæ et Pini Compositus, B.P.C. (Pastill. Diamorph. et Pini Co.).—Compound Diamorphine and Pine Pastilles. Each pastille contains $\frac{1}{48}$ gr. of diamorphine hydrochloride, $\frac{1}{4}$ min. of oil of pumilio pine and $\frac{1}{8}$ gr. of terpin hydrate.

DIGITALIS FOLIUM (Digitalis Leaves).

The leaf of *Digitalis purpurea* Linn., rapidly dried between 55° and 60° as soon as possible after collection.

STORAGE.

Should be stored in well-closed containers and protected from moisture.

DISPENSING.

When Digitalis Folium, Digitalis, Digitalis Folia or Pulvis Digitalis is prescribed *Digitalis Pulverata* must be dispensed.

PREPARATIONS.

Digitalis Pulverata, B.P. (Digit. Pulverat.).—Powdered Digitalis. Digitalis leaf in No. 20 powder of ascertained strength, which is stated in units, one unit corresponding to the activity of 0·08 gm. of the international standard digitalis powder. Loss on drying at 100°, not more than 8%. For therapeutic administration, the strength is adjusted to 10 units per gramme by admixture with exhausted digitalis leaf or with a weaker powdered digitalis. It should be stored in air-tight containers. *Dose*—For a single administration, 3 to 10 gr. (0·2 to 0·6 gm.), equivalent to 2 to 6 units of activity; for repeated administration, ½ to 1½ gr. (0·03 to 0·1 gm.), equivalent to 0·3 to 1 unit of activity.

Infusum Digitalis Recens, B.P. (Inf. Digit. Rec.).—Fresh Infusion of Digitalis. *Syn.*—Infusum Digitalis; Infusion of Digitalis. It is prepared with the equivalent of 0·5% w/w of international standard digitalis powder. 120 mils or 4 fl. ozs. contains 6 units of activity; it is one-twentieth the strength of tincture of digitalis. When Infusum Digitalis or infusion of digitalis is prescribed, fresh infusion of digitalis shall be dispensed. *Uses*—Cardiac Tonic. *Dose*—1½ to 5 fl. dr. (6 to 20 mils); *single dose*—1 to 4 fl. oz. (30 to 120 mils).

Pilulæ Digitalis Compositæ, B.P.C. (Pil. Digit. Co).—Compound Digitalis Pills. *Syn.*—Pilulæ Digitalis cum Scilla; Guy's Pills; Niemeyer's Pills. Each pill contains 1 gr. each of powdered digitalis, squill, and pill of mercury. *Uses*—Cardiac Tonic. *Dose*—1 or 2 pills.

Tinctura Digitalis, B.P. (Tinct. Digit.).—Tincture. Each millilitre possesses one unit of activity and is equivalent to 0·08 gm. of the international standard digitalis powder. It may be prepared from digitalis leaf by percolation with alcohol (70%), the product being adjusted to the required strength, or it may be prepared from powdered digitalis by percolation without

subsequent adjustment or by maceration. $1\frac{1}{2}$ fl. dr. or 6 mils contains 6 units of activity. *Uses*—Cardiac tonic. *Dose*—5 to 15 min. (0·3 to 1 mil) ; *single dose*—$\frac{1}{2}$ to $1\frac{1}{2}$ fl. dr. (2 to 6 mils).

DIGOXINUM (Digoxin).

CHARACTERS.

A crystalline glycoside obtained from *Digitalis lanata*, Ehrh. Almost *insoluble* in water, more *soluble* in alcohol.

USES.

Given orally for auricular fibrillation.

DISPENSING.

A solution in alcohol (70%) is sterilized by heating in an autoclave. For intravenous use, a solution containing 0·0005 gm. in 1 mil of alcohol (70%), is diluted with 10 times its volume of Physiological solution of Sodium Chloride.

DOSE.

Oral—initial dose—$\frac{1}{60}$ to $\frac{1}{40}$ gr. (0·001 to 0·0015 gm.); oral-maintenance dose—$\frac{1}{240}$ gr. twice daily (0·00025 gm.).

Intravenous—$\frac{1}{120}$ to $\frac{1}{60}$ gr. (0·0005 to 0·001 gm.).

DIODONUM (Diodone).

SYNONYMS AND PROPRIETARY NAMES.

Per-Abrodil (*Bayer Products, London*), Pyelosil (*Glaxo Laboratories, London*).

CHARACTERS.

A clear colourless liquid, *soluble* in water.

USES.

A contrast medium for pyelography.

DOSE.

20 mil of a 35% w/v solution, by injection.

DIPHENANUM (Diphenan).

SYNONYMS AND PROPRIETARY NAMES.

p-Benzylphenyl Carbamate, Butolan (*Bayer Products, London*), Oxylan (*Burroughs Wellcome, London*).

CHARACTERS.

A white, tasteless, crystalline compound, slightly *soluble* in water.

USES.

For removal of threadworms.

DOSE.

$7\frac{1}{2}$ to 15 gr. (0·5 to 1·0 gm.), three times daily for one week.

DITHRANOLUM (Dithranol).

SYNONYMS AND PROPRIETARY NAMES.

Anthrarobin, Anthralin (*Abbott Laboratories, London*), Cignolin (*Bayer Products, London*), Derobin (*Glaxo Laboratories, London*).

CHARACTERS.

Yellow crystals, *insoluble* in water, *soluble* in alcohol, ether, chloroform, and fixed oils.

USES.

As a stimulant and parasiticide in skin diseases, in the form of an ointment.

EMETINÆ ET BISMUTHI IODIDUM (Emetine and Bismuth Iodide).

CHARACTERS.

A reddish-orange powder, odourless, with a bitter acrid taste. Contains 25 to 28% emetine.

Insoluble in water and alcohol.

STORAGE.

In well closed containers protected from light.

USES.

A specific for the treatment of amœbic dysentery.

DISPENSING.

Pills and tablets should be enteric coated.

DOSE.

1 to 3 gr. (0·06 to 0·2 gm.).

EMETINÆ HYDROCHLORIDUM (Emetine Hydrochloride).

CHARACTERS.

A colourless, crystalline powder, odourless, with bitter taste. Turns yellow on exposure to light.

Soluble in water and alcohol.

USES.

Emetic when administered orally (*Dose*— $\frac{1}{10}$ gr.). Specific for amœbic dysentery (parenteral).

DISPENSING.

Capsules containing emetine hydrochloride should be treated with formaldehyde solution, and pills and tablets should be enteric coated. Solutions for injection may be sterilized by tyndallization or filtration and the containers should comply with the tests for limit of alkalinity of glass.

DOSE.

By injection, $\frac{1}{2}$ to 1 gr. (0·03 to 0·06 gm.).

EPHEDRINA (Ephedrine).

SYNONYM.

Ephedrine hemihydrate.

CHARACTERS.

Colourless, non-deliquescent crystals.

Soluble readily in water, alcohol, ether; a chloroform solution is turbid due to separation of water. Soluble in 20 parts of glycerin, 25 of olive oil, and 100 of liquid paraffin. The last solution is not clear and water separates.

USES.

Vasoconstrictor, bronchodilator in asthma.

DISPENSING.

This ephedrine hemihydrate is not hygroscopic. Anhydrous ephedrine is hygroscopic, but forms (if dry) clear solutions in oils, chloroform and liquid paraffin.

DOSE.

$\frac{1}{4}$ to $1\frac{1}{2}$ gr. (0·016 to 0·1 gm.).

EPHEDRINÆ HYDROCHLORIDUM (Ephedrine Hydrochloride).

CHARACTERS.

Colourless, odourless crystals.

Soluble 1 in 5 parts of water, and 1 in 5 parts of alcohol.

USES.

Vasoconstrictor, bronchodilator in asthma.

DISPENSING.

Solutions for injection may be sterilized by autoclaving, or by filtration.

For aqueous nasal sprays ephedrine hydrochloride is usually employed, while the base, ephedrine, is used for oily sprays and ointments.

PREPARATIONS.

Elixir Ephedrinæ Hydrochloridi, B.P.C. (Elix. Ephed. Hydrochlor.).—Elixir of Ephedrine Hydrochloride. Each fluid drachm contains ¼ gr. of ephedrine hydrochloride with distilled water, glycerin, spirit of chloroform, tincture of lemon, alcohol (90%) and syrup, coloured with compound solution of tartrazine. *Dose*—½ to 2 fl. dr. (2 to 8 mils).

Nebula Adrenalinæ et Ephedrinæ, B.P.C. (Neb. Adrenal. et Ephed.).—Adrenaline and Ephedrine Spray. Adrenaline, as solution of adrenaline hydrochloride, 1 in 8000, ephedrine hydrochloride, about 1 in 45, and glycerin of phenol, in cinnamon water.

Nebula Adrenalinæ et Ephedrinæ Oleosa, B.P.C. (Neb. Adrenal. et Ephed. Oleos.).—Oily Adrenaline and Ephedrine Spray. Adrenaline, 1 in 10,000, and ephedrine, 1 in 50, with menthol and eucalyptol, in acidified dehydrated alcohol, castor oil and arachis oil.

Nebula Ephedrinæ Composita, B.P.C. (Neb. Ephed. Co.).—Compound Ephedrine Spray. Ephedrine, 1% w/v, with menthol, camphor, oil of thyme and light liquid paraffin.

ERGOMETRINA (Ergometrine).

SYNONYMS.

Ergonovine (N.N.R.), Ergotocin, Ergobasine, Ergostetrine.

CHARACTERS.

Colourless, hygroscopic crystals, becoming coloured on exposure to air.

Soluble slightly in water.

USES.

Given after parturition, to check post-partum hæmorrhage.

DOSE.

Oral, $\frac{1}{120}$ to $\frac{1}{60}$ gr. (0·0005 to 0·001 gm.); intramuscular injection $\frac{1}{240}$ to $\frac{1}{120}$ gr. (0·00025 to 0·0005 gm.); intravenous injection, $\frac{1}{480}$ to $\frac{1}{240}$ gr. (0·000125 to 0·00025 gm.).

ERGOTA (Ergot).

SYNONYM.

Secale cornutum.

CHARACTERS.

Ergot is the sclerotium of *Claviceps purpurea* Talasne, developed in the ovary of the rye *Secale cereale* Linn. It should contain not less than 0·05% total alkaloids of ergot, calculated as ergotoxine.

STORAGE.

Ergot should be thoroughly dried, kept entire, and stored in a cool place.

USES.

To excite uterine contractions. Largely used to check uterine hæmorrhage.

DISPENSING.

When ergot, Pulvis Ergotæ, or powdered ergot is prescribed, Ergota Præparata should be dispensed. The liquid extract loses activity rapidly when diluted with water and should therefore be dispensed undiluted, or in mixtures freshly prepared.

PREPARATIONS.

Ergota Præparata, B.P. (Ergot. Præp.).—Prepared Ergot. Defatted ergot, in moderately fine powder, adjusted by admixture with exhausted ergot, or ergot of ascertained strength, to contain 0·1 per cent. of the total alkaloids of ergot, calculated

as ergotoxine ; 15 gr. contains about $\frac{1}{60}$ gr., and 1 gm. contains about 0·001 gm., of total alkaloids. It should be stored in air-tight containers. *Dose*—5 to 15 gr. (0·3 to 1 gm.).

Extracta Ergotæ Liquidum, B.P. (Ext. Ergot. Liq.).—Liquid Extract of Ergot. It is prepared from defatted ergot with alcohol (50%) acidified with tartaric acid, concentration, if necessary, being effected under reduced pressure at a temperature not exceeding 40°, and is adjusted to contain, when fresh, 0·06% w/v of the total alkaloids of ergot, calculated as ergotoxine ; 20 min. contains about $\frac{1}{90}$ gr., and 1·2 mil contains 0·0007 gm. It deteriorates rapidly on keeping and is not used when the alkaloid content has fallen below 0·04% w/v. It should be stored in small, completely filled bottles, in as cool a place as possible. *Dose*—10 to 20 min. (0·6 to 1·2 mil).

ERGOTOXINÆ ETHANSULPHONAS (Ergotoxine Ethansulphonate).

CHARACTERS.

Colourless, acicular crystals.

Sparingly *soluble* in water, more *soluble* in alcohol (90%).

USES.

As for ergot. Administered often by injection.

DISPENSING.

Solutions for injection are prepared by dissolving in sterilized water immediately before use, and containers should comply with limit tests for alkalinity of glass. The solution should be stored protected from light.

DOSE.

By subcutaneous or intramuscular injection $\frac{1}{120}$ to $\frac{1}{60}$ gr. (0·0005 to 0·001 gm.).

ERYTHRITYLIS TETRANITRAS DILUTUS (Diluted Erythrityl Tetranitrate).

SYNONYMS.

Erythrityl Tetranitrate (50%), Erythrol Tetranitrate (50%).

CHARACTERS.

A mixture of equal weights of erythrityl tetranitrate and lactose. A sweet white powder.

USES.

Vasodilator.

DISPENSING.

When erythrityl tetranitrate is prescribed, twice the prescribed amount of Diluted Erythrityl Tetranitrate must be dispensed. Usually administered as tablets which should be chewed and not swallowed whole.

DOSE.

$\frac{1}{2}$ to 2 gr. (0·03 to 0·12 gm.), representing $\frac{1}{4}$ to 1 gr. (0·016 to 0·06 gm.) of pure erythrityl tetranitrate.

EUCALYPTOL (Eucalyptol).

SYNONYM.

Cineole.

CHARACTERS.

A colourless liquid with odour of oil of eucalyptus.

USES.

Antiseptic.

DOSE.

1 to 3 min. (0·06 to 0·2 mil).

PREPARATIONS.

Nebula Eucalyptolis Composita, B.P.C. (Neb. Eucalyp. Co.).—Compound Eucalyptol Spray. *Syn.*—Nebula Thymolis Composita. Eucalyptol, 8% v/v, with camphor, menthol and thymol in light liquid paraffin.

Pastilli Mentholis et Eucalyptolis, B.P.C. (Pastill. Menthol. et Eucalyp.).—Menthol and Eucalyptol Pastilles. Each pastille contains $\frac{1}{20}$ gr. of menthol and $\frac{1}{2}$ min. of eucalyptol.

FERRUM (Iron).

Iron is metallic iron in the form of fine bright wire, having a diameter of about 0·1 mil (No. 42 standard wire gauge).

The different preparations of this substance vary in their actions. Pure iron, for example, acts simply as a Tonic and hæmatinic or blood improver, whilst the acid preparations are generally powerful astringents as well. Iron forms a dark ink when ordered with any of the bitter infusions, except those of Quassia and Calumba. The same remark applies to all astringent vegetable tinctures. Iron, like arsenic, should be prescribed to be taken after meals and freely diluted.

PREPARATIONS.

Ferrum Redactum. (Reduced Iron). — A grey-black powder, containing at least 80% of metallic iron. Used in the treatment of anæmia due to deficiency of hæmoglobin. Tonic. *Dose*—1 to 10 gr.

Syrupus Ferri Iodidi (5% w/w FeI_2).—A colourless syrup prepared by shaking iodine with water until the reaction is completed, heating and filtering into hypophosphorous acid, washing the filter with water until filtrate measures the required amount, and adjusting the volume with syrup. 2 dr. contains $7\frac{1}{2}$ gr. of ferrous iodide. It should be kept in well-closed clear glass bottles. *Dose*—$\frac{1}{2}$ to 2 dr. (2 to 8 mils); for a child 1 year old, 2 min.

Syrupus Ferri Phosphatis Compositus.—*Syn.*—Parrish's Food; Parrish's Syrup; Chemical Food. A deep red pleasantly acid syrup, prepared by dissolving iron in phosphoric acid, incorporating calcium carbonate, potassium bicarbonate, sodium phosphate, sucrose, orange-flower water of commerce undiluted, colouring with cochineal, and adjusting to the requisite volume with water. 2 dr. contains $1\frac{1}{6}$ gr. anhydrous ferrous phosphate, $1\frac{3}{4}$ gr. tricalcium phosphate. Tonic. *Dose*—$\frac{1}{2}$ to 2 dr. (2 to 8 mils).

Syrupus Ferri Phosphatis cum Quinina et Strychnina.—*Syn.*—Easton's Syrup. A clear fluorescent syrup, made by dissolving iron wire in concentrated phosphoric acid, and in this dissolving quinine sulphate and strychnine, and filtering into a mixture of glycerin and syrup and adding water, the whole containing 1 gr. anhydrous ferrous phosphate, $\frac{4}{5}$ gr. quinine sulphate, and $\frac{1}{80}$ gr. strychnine hydrochloride in 1 dr. Tonic. *Dose.*—$\frac{1}{2}$ to 1 dr. (2 to 4 mils).

Ferri Carbonas Saccharatus.—Saccharated Iron Carbonate. Ferrous carbonate, more or less oxidized and mixed with glucose. Contains not less than 50% ferrous salts calculated as ferrous carbonate, $FeCO_3$. A greenish-brown powder,

cohering in little lumps, prepared by adding sodium carbonate to a solution of ferrous sulphate in liquid glucose and water, mixing the washed precipitate with liquid glucose and drying. Tonic. *Dose*—10 to 30 gr. (0·6 to 2 gm.).

Ferri et Ammonii Citras.—Iron and Ammonium Citrate, in transparent ruby scales, may be prepared by mixing solutions of ferric sulphate and ammonia and dissolving the freshly precipitated ferric hydroxide thus formed in solution of citric acid, and, after the addition of ammonia, evaporating. Tonic. *Dose*—20 to 40 gr. (1·3 to 2·6 gm.) in solution.

Ferri et Quininæ Citras.—Iron and Quinine Citrate. 15% Quinine. In greenish-yellow scales, being a citrate of quinine, iron and ammonium, prepared by dissolving the ferric hydroxide (formed as in the last preparation) in citric acid, adding quinine (prepared by precipitating the sulphate by ammonia), neutralizing with ammonia, and evaporating. 15 gr. contain 2¼ gr. of quinine. Tonic. *Dose*—5 to 10 gr. (0·3 to 1 gm.).

FERRI SULPHAS (Ferrous Sulphate).

CHARACTERS.

Transparent, pale green crystals, or as a pale bluish-green granular, crystalline powder.

Soluble 1 part in 1·5 of water, *insoluble* in alcohol (90%).

USES.

Tonic and astringent.

DOSE.

1 to 5 gr. (0·06 to 0·3 gm.).

PREPARATIONS.

Ferri Sulphas Exsiccatus, B.P.—Exsiccated Ferrous Sulphate. Contains not less than 80% anhydrous $FeSO_4$. A greyish powder, prepared by heating Ferri Sulphas, $FeSO_4$, $7H_2O$. 2½ gr. = 4 gr. Ferri Sulphas. *Dose*—½ to 3 gr. (0·03 to 0·2 gm.). (In—Pil. Aloes et Ferri and Pil. Ferri Carb.)

Pilula Aloes et Ferri, B.P.—Contains exsiccated ferrous sulphate, aloes, cinnamon, cardamon, ginger, and syrup of liquid glucose. *Dose*—4 to 8 gr. (0·25 to 0·5 gm.).

Pilula Ferri Carbonatis, B.P.—Pill of Iron Carbonate. Blaud's Pill, Iron Pill, Pilula Ferri. Prepared by mixing exsiccated ferrous sulphate, liquid glucose and water, adding

exsiccated sodium carbonate, and, when reaction ceases, adding gum acacia and tragacanth. Tonic, emmenagogue. *Dose*—5 to 30 gr. (0·3 to 2 gm.).

Liquor Ferri Perchloridi, B.P.—Solution of Ferric Chloride. A solution of ferric chloride in distilled water, of strength 15% w/v of $FeCl_3$. It may be obtained by the oxidation of ferrous chloride, prepared by the interaction of diluted hydrochloric acid and iron. Tonic and astringent. *Dose*—5 to 15 min. (0·3 to 1 mil). (Used in preparing Injectio Ferri.)

Mistura Ferri Composita, B.P.C. (Mist. Ferr. Co.).—Compound Iron Mixture. *Syn.*—Griffith's Mixture. Each fluid ounce contains ferrous carbonate, equivalent to about 3 gr. of ferrous sulphate, with potassium carbonate, myrrh, acacia, liquid glucose, spirit of nutmeg and rose water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

FILIX MAS (Male Fern).

The rhizome and frond bases of *Dryopteris Filix-mas* (Linn.) Schott.

Contains a yellow amorphous substance termed filmarone, to which the properties of male fern as a vermifuge are attributed.

USES.

Tænicide.

DISPENSING.

Generally employed as Extractum Filicis. This is administered in mixture form, or in capsules. Male fern extract may be emulsified by an equal weight of acacia, or with $\frac{1}{6}$ of its volume of Tincture of Senega.

DOSE.

60 to 180 gr. (4 to 12 gm.).

PREPARATION.

Extractum Filicis.—Filicin. Extract of Male Fern. *Syn.*—Liquid Extract of Male Fern, Oleoresina Aspidii. A thick, dark-green, oily liquid, being the oleo-resin prepared by extraction from the male fern rhizome by percolating it with ether, and evaporation of the solvent, assaying, and, if necessary, adding olive oil to make the strength 25% w/w of filicin.

Anthelmintic—for tænia solium. *Dose*—45 to 90 min. (3 to 6 mils), in emulsion.

FLUORESCEINUM SOLUBILE (Soluble Fluorescein).

CHARACTERS.

An orange-red powder, odourless, tasteless, giving a well-marked green fluorescence in solution.

Soluble 1 part in 1 of water, 1 part in 50 of alcohol (90%).

USES.

As a diagnostic agent for dilineating corneal lesions.

FŒNICULUM (Fennel).

The dried ripe fruits of cultivated plants of *Fœniculum vulgare* Mill.

USES.

Aromatic and carminative. Fennel water mixed with sodium bicarbonate and syrup is given to infants for the relief of flatulence.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

PREPARATIONS.

Aqua Fœniculi Concentrata, B.P.C. (Aq. Fœnic. Conc.).—Concentrated Fennel Water. Oil of Fennel, 1 in 50. One part added to 30 parts of distilled water yields a preparation which is approximately equivalent in strength to distilled fennel water, but contains 1·5% v/v of alcohol (90%). *Dose*—5 to 15 min. (0·3 to 1 mil).

Aqua Fœniculi Destillata, B.P.C. (Aq. Fœnic. Dest.).—Distilled Fennel Water. Fennel, 1 in 10. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

GELATINUM (Gelatin).

CHARACTERS.

In translucent, almost colourless sheets or shreds, being the air-dried product of the action of boiling water on such animal tissues as skin, tendons, ligaments, and bones.

USES.

For making suppositoria glycerini, lamellæ, gelatin of zinc.

PREPARATION.

Gelatinum Zinci.—Gelatin of Zinc. *Syn.*—Unna's Paste. A very firm jelly made by incorporating Zinc Oxide in a base of gelatin, glycerin and water. It must be melted prior to use.

GENTIANA (Gentian).

The dried rhizome and root of *Gentiana lutea.*

USES.

Bitter tonic without astringency.

DOSE.

10 to 30 gr. (0·6 to 2·0 gm.).

PREPARATIONS.

Infusum Gentianæ Compositum Concentratum, B.P. (Inf. Gent. Co. Conc.).—Concentrated Compound Infusion of Gentian. Gentian and dried bitter-orange peel, about 1 in 10, and lemon peel, about 1 in 5, extracted with alcohol (25%). This concentrated infusion when diluted with seven times its volume of distilled water yields a preparation which is approximately equivalent in strength, but not in flavour, to fresh compound infusion of gentian and differs also in containing a small proportion of alcohol. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

Infusum Gentianæ Compositum Recens, B.P. (Inf. Gent. Co. Rec.).—Fresh Compound Infusion of Gentian. Gentian and dried bitter-orange peel, 1 in 80, and lemon peel, 1 in 40. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Mistura Gentianæ Alkalina, B.P.C. (Mist. Gent. Alk.).—Alkaline Gentian Mixture. *Syn.*—Mistura Gentianæ cum Soda. Each fluid ounce contains 15 gr. of sodium bicarbonate and 5 gr. of ammonium carbonate, with syrup of orange and compound infusion of gentian. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Tinctura Gentianæ Composita, B.P. (Tinct. Gent. Co.).—Compound Tincture of Gentian. Gentian, 1 in 10, with dried bitter-orange peel and cardamom, prepared by maceration with alcohol (45%). *Dose*—½ to 1 fl. dr. (2 to 4 mils).

GLYCERINUM (Glycerin).

CHARACTERS.

A colourless, viscous, odourless, sweet liquid.
Miscible with water and alcohol.

USES.

Demulcent, laxative. Commonly employed as a sweetening agent. In pastilles it is used as an emollient for the throat.

Externally it is applied as an emollient in many creams and jellies.

DISPENSING.

Glycerin may be sterilized by heating at 150° C. for 1 hour.

DOSE.

1 to 2 fl. dr. (4 to 8 mils); for rectal injection, ½ to 2 dr. (2 to 8 mils).

PREPARATION.

Suppositoria Glycerini, B.P. (70%).—Translucent cones, prepared by soaking gelatin 14 in a little water till it becomes soft, and then dissolving it in glycerin 70 and evaporating till the mixture weighs 100 parts, when it is poured into moulds capable of holding 30, 60, or 120 gr., or other capacity. Each suppository contains 70% of glycerin. (Used for inserting into the rectum for constipation.)

GLYCERYLIS TRINITRATIS, LIQUOR (Solution of Glyceryl Trinitrate).

SYNONYMS.

Solution of Nitroglycerin, Solution of Trinitrin, Liquor Trinitrini.

CHARACTERS.

An alcoholic (90%) solution containing 1% w/v glyceryl trinitrate.

USES.

Vasodilator.

DISPENSING.

Often administered as Tabella Glyceryl Trinitratis, which should be chewed, not swallowed whole.

DOSE.

$\frac{1}{2}$ to 2 min. (0·03 to 0·12 mil).

NOTE.—If Liquor Glyceryl Trinitratis is dispensed in an aqueous vehicle, oily drops of glyceryl trinitrate will be deposited.

PREPARATION.

Tabella Glycerylis Trinitratis, B.P..—Tablet of Glyceryl Trinitrate. *Syn.*—Trinitrin Tablets, Tablets of Nitroglycerin. Tablets with a chocolate basis, each containing $\frac{1}{120}$ gr. (0·0005 gm.) of glyceryl trinitrate. *Dose*—1 to 2 tablets.

GLYCYRRHIZA (Liquorice).

The root and subterranean stem of *Glycyrrhiza glabra* Linn. and other species, either peeled or unpeeled.

Active principle—glycyrrhizin.

USES.

Demulcent and mild expectorant. Extractum Glycyrrhizæ enters into the composition of cough lozenges and pastilles. The liquid extract is used in cough mixtures and to disguise the taste of nauseous substances—alkali iodides and ammonium chloride. Liquorice extracts should only be prescribed in neutral or alkaline media.

DOSE.

15 to 60 gr. (1 to 4 gm.).

PREPARATIONS.

Extractum Glycyrrhizæ, B.P. (Ext. Glycyrrh.).—Extract of Liquorice. A soft aqueous extract. *Dose*—10 to 30 gr. (0·6 to 2 gm.).

Extractum Glycyrrhizæ Liquidum, B.P. (Ext. Glycyrrh. Liq.).—Liquid Extract of Liquorice. An aqueous extract adjusted to a specific gravity of 1·200 and preserved with alcohol. *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

Pulvis Glycyrrhizæ Compositus, B.P. (Pulv. Glycyrrh. Co.).—Compound Powder of Liquorice. Peeled liquorice and senna leaf, of each 16%, with fennel, sublimed sulphur and sucrose. *Dose*—1 to 2 dr. (4 to 8 gm.).

Trochisci Glycyrrhiza, B.P.C. (Troch. Glycyrrh.).—Liquorice Lozenges. *Syn.*—Brompton Cough Lozenges. Each lozenge contains 3 gr. of extract of liquorice and $\frac{1}{2}$ min. of oil of anise.

GUAIACOL (Guaiacol).

CHARACTERS.

A colourless, oily, highly refractive liquid, or as colourless crystals.

Soluble 1 part in 80 of water, *miscible* with alcohol.

USES.

Antiseptic and dèodorant.

DOSE.

5 to 10 min. (0·3 to 0·6 mil).

HAMAMELIS (Hamamelis).

SYNONYMS.

Hamamelidis Folia, Hamamelis Leaves, Witch Hazel Leaves.

The dried leaves of *Hamamelis virginiana* Linn. Also used in the fresh condition.

USES.

A local astringent and hæmostatic. The extract in the form of suppositories and ointment is used for piles.

PREPARATIONS.

Extractum Hamamelidis, B.P.C. (Ext. Hamam.).—Extract of Hamamelis. *Syn.*—Hamamelin; Hamamelidin. A dry alcoholic extract. *Dose*—1 to 5 gr. (0·06 to 0·3 gm.).

Extractum Hamamelidis Liquidum, B.P. (Ext. Hamam. Liq.).—Liquid Extract of Hamamelis. 1 in 1. It is prepared from the dried leaves with alcohol (45%). *Dose*—½ to 1 fl. dr. (2 to 4 mils).

Pasta Hamamelidis, B.P.C. (Past. Hamam.).—Hamamelis Paste. *Syn.*—Witch Hazel Cream. A non-greasy stearate cream containing about 50% w/v of solution of hamamelis.

Liquor Hamamelidis, B.P.C. (Liq. Hamam.).—Solution of Hamamelis. *Syn.*—Distilled Witch Hazel. A 1 in 1 solution prepared by distillation from the fresh leaf.

Suppositorium Hamamelini et Zinci Oxidi, B.P.C. (Supp. Hamam. et Zinc. Oxid).—Hamamelin and Zinc Oxide Suppository. Each suppository weighs 30 gr. (2 gm.) and contains 3 gr. of extract of hamamelis and 10 gr. of zinc oxide.

Unguentum Hamamelidis, B.P.C. (Ung. Hamam.).—Hamamelis Ointment. Liquid Extract of hamamelis, 10%, in wool fat and yellow soft paraffin.

HEPATIS, EXTRACTUM LIQUIDUM (Liquid Extract of Liver).

Liquid Extract of Liver is a selected fraction of an alcoholic extract of ox or sheep liver, dissolved in a mixture of glycerin, alcohol and distilled water. It contains the specific principle which increases the number of red blood corpuscles in the blood of persons suffering from pernicious anæmia. It should be stored in a cool place as it may lose activity, and should be used as soon as possible.

DOSE.

1 fl. oz. (30 mils). (1 fl. oz. contains the equivalent of 8 oz. of fresh liver.)

HEPATIS, EXTRACTUM SICCUM (Dry Extract of Liver)

Contains the same principle as the liquid extract and is made in a similar manner, except that the powder is reduced to a dry powder by evaporation *in vacuo*.

CHARACTERS.

A light brown, very hygroscopic powder, with a faint meat-like odour and a salty meat-like taste.

Soluble in water, *insoluble* in alcohol.

STORAGE.

It should be stored in sealed glass tubes, placing in each the quantity equivalent to 225 gm. of the original liver.

DOSE.

The quantity equivalent to ½ lb. (225 gm.) of fresh liver.

HEXAMINA (Hexamine).

SYNONYMS AND PROPRIETARY NAMES.

Hexamethylenetetramine, Urotropine, Aminoform, Formin, Formamine, Urisol, Metramine (*Oppenheimer, London*), Uritrone, Vesalvine (*Martindale, London*).

CHARACTERS.

Colourless, odourless crystals, or crystalline powder.

Soluble 1 part in 1·5 of water, and 1 part in 8 of alcohol (90%).

USES.

Urinary tract disinfectant. Frequently prescribed after the urine has been rendered acid with sodium acid phosphate.

DISPENSING.

Solutions for injection may be sterilized by filtration.

DOSE.

10 to 30 gr. (0·6 to 2·0 gm.).

HEXOBARBITONUM (Hexobarbitone).

SYNONYMS AND PROPRIETARY NAMES.

Methexenyl, Hexanastab-oral (*Boots, Nottingham*), Evipan (*Bayer, London*), Hexobarbital.

CHARACTERS.

Colourless crystals, odourless.

Soluble 1 in about 3000 parts of water, *soluble* in dehydrated alcohol, methyl alcohol, acetone, benzene, chloroform, and ether. *Soluble* in aqueous alkali hydroxides, but not in alkali carbonate solutions.

USES.

An effective hypnotic, with rapid action which lasts a relatively short time.

DOSE.

4 to 8 gr. (0·25 to 0·5 gm.).

PREPARATION.

Hexobarbitonum Solubile (Soluble hexobarbitone). *Syn.* and *Prop. Names*—Soluble hexobarbital, Methexenyl Sodium, Cyclonal Sodium (*Pharmaceutical Specialities* (*May & Baker*) *Ltd., London*), Evipan Sodium (*Bayer, London*), Hexanastab (*Boots, Nottingham*). A white hygroscopic powder, readily *soluble* in water. Solutions for parenteral use are prepared by dissolving in sterile water immediately before use. An aqueous solution is not stable in air, and deposits hexobarbitone. *Uses*—An effective anæsthetic, whose action is of short duration.

Administered by intravenous, intramuscular injection or per rectum. *Doses*—By injection—3 to 15 gr. (0·2 to 1·0 gm.); by rectal injection, 30 to 60 gr. (2·0 to 4·0 gm.).

HISTAMINÆ PHOSPHAS ACIDUS (Histamine Acid Phosphate).

CHARACTERS.

Colourless, odourless crystals.
Soluble 1 in $4\frac{1}{2}$ parts of water.

USES.

In treatment of rheumatism; for the differential diagnosis of pernicious and secondary anæmias.

DISPENSING.

Solutions for injection may be sterilized by heating in an autoclave or by filtration. The containers must comply with the limit test for alkalinity of glass.

DOSE.

By subcutaneous injection, $\frac{1}{120}$ to $\frac{1}{60}$ gr. (0·0005 to 0·001 gm.).

HOMATROPINÆ HYDROBROMIDUM (Homatropine Hydrobromide).

CHARACTERS.

A colourless, odourless, crystalline powder.
Soluble 1 part in 6 of water, and 1 part in 18 of alcohol (90%).

USES.

Mydriatic. Its effect on the eye is similar to that of atropine, but its action is more rapid, persists for a shorter time and passes off in about 24 hours.

DISPENSING.

Solutions for injection may be sterilized by heating with a bactericide or filtration, and the containers should comply with the limit tests for alkalinity of glass.

DOSE.

$\frac{1}{64}$ to $\frac{1}{32}$ gr. (0·001 to 0·002 gm.).

HYDRARGYRUM (Mercury).

CHARACTERS.

A lustrous silver-white fluid metal.

DOSE.

$\frac{1}{2}$ to 3 gr. (0·03 to 0·2 gm.); by intramuscular injection $\frac{1}{2}$ to 1 gr. (0·03 to 0·06 gm.).

PREPARATIONS.

Hydrargyrum cum Creta (1 in 3).—*Syn.*—Grey Powder. A greyish-blue powder prepared by rubbing mercury with prepared chalk until metallic globules cease to be visible when examined under a lens magnifying 4 diameters. Purgative. *Dose*—1 to 5 gr. (0·06 to 0·3 gm.); for a child 1 year old, 1 gr.

Injectio Hydrargyri.—Injection of Mercury, 10% w/v. *Syn.*—Mercurial Cream. A sterile oily suspension of mercury, in a basis of wool fat, olive oil, and containing camphor and creosote. Antisyphilitic. *Dose*—By intramuscular injection, 5 to 10 min. (0·3 to 0·6 mils) (10 min. contains 1 gr. of mercury).

Pilulæ Colchici et Hydrargyri Compositæ, B.P.C. (Pil. Colch. et Hydrarg. Co.).—Compound Colchicum and Mercury Pills. *Syn.*—Brodie's Gout Pills. Each pill contains $\frac{1}{2}$ gr. of dry extract of colchicum and $1\frac{1}{3}$ gr. each of pill of mercury, compound extract of colocynth and extract of rhubarb. *Dose*—1 or 2 pills.

Pilulæ Digitalis Compositæ, B.P.C. (Pil. Digit. Co.).—Compound Digitalis Pills. *Syn.*—Pilulæ Digitalis cum Scilla; Guy's Pills; Niemeyer's Pills. Each pill contains 1 gr. each of powdered digitalis, squill and pill of mercury. *Dose*—1 or 2 pills.

Pilula Hydrargyri (1 in 3. 33%).—*Syn.*—Blue Pill. Prepared by rubbing mercury with syrup, liquid glucose, glycerin, and liquorice in fine powder. Purgative. *Dose*—4 to 8 gr. (0·25 to 0·5 gm.).

Unguentum Hydrargyri (30%).—Prepared by rubbing together mercury, benzoinated lard and suet. Used to introduce mercury into the system through the skin. Antisyphilitic. (There are 6 ointments bearing the name of mercury.)

Unguentum Hydrargyri Dilutum.—Dilute ointment of mercury, 33% of Ointment of Mercury in Simple Ointment. When Mercury Ointment, Mercurial Ointment, or Blue Ointment is prescribed or demanded, Dilute Ointment of Mercury shall be dispensed or supplied, unless, on enquiry, it is ascertained that Ointment of Mercury is required.

Unguentum Hydrargyri Compositum (12% of Hg).—*Syn.*—Scott's Dressing. A bluish ointment, consisting of ointment of mercury, yellow beeswax, olive oil, and camphor. (This is a substitute for Scott's Ointment, by which name it is also known.)

Unguentum Hydrargyri Nitratis Forte.—Strong Ointment of Mercuric Nitrate. *Syn.*—Mercuric Nitrate Ointment. Prepared by adding a solution of mercury in nitric acid to a hot mixture of lard and olive oil. Known also as Citrine Ointment from its pale lemon colour. A local alternative, astringent, and stimulant.

Unguentum Hydrargyri Nitratis Dilutum (20% Ung.).—*Syn.*—Diluted Ointment of Nitrate of Mercury. 1 of Ung. Hydrarg. Nit. Forte and 4 of soft paraffin (yellow).

HYDRARGYRI IODIDI RUBRUM (Red Mercuric Iodide).

SYNONYM.

Mercuric Iodide.

CHARACTERS.

A scarlet red powder.

Almost *insoluble* in water, *soluble* 1 part in 300 of alcohol (90%).

USES.

Antisyphilitic. In solution with potassium iodide, a powerful antiseptic.

DISPENSING.

Solutions in water or alcohol may be obtained by the addition of $\frac{4}{5}$ of its weight of potassium iodide.

DOSE.

$\frac{1}{32}$ to $\frac{1}{16}$ gr. (0·002 to 0·004 gm.).

PREPARATIONS.

Liquor Arseni et Hydrargyri Iodidi, B.P. (Liq. Arsen. et Hydrarg. Iod.).—Solution of Arsenous and Mercuric Iodides. *Syn.*—Donovan's Solution. It contains 1% w/v of red mercuric iodide, and total arsenic equivalent to 1% w/v of arsenic triiodide, in distilled water. 15 min. contains about $\frac{1}{7}$ gr., and 1 mil contains the equivalent of about 0·01 gm. of each salt. The arsenous compound in the solution is rapidly oxidized to the arsenic state in contact with air. The solution should be freshly prepared or, if not used immediately, it should be

stored in well-filled containers and protected from light. *Dose*—5 to 15 min. (0·3 to 1 mil).

Solvellæ Hydrargyri Iodidi, B.P.C. (Solv. Hydrarg. Iod.).—Mercuric Iodide Solution Tablets. *Syn.*—Soluble Biniodide Tablets. Each tablet contains $8\frac{3}{4}$ gr. of mercuric iodide, with potassium iodide and eosin; one tablet dissolved in 20 fl. ozs. of water forms a solution containing 1 in 1000 of mercuric iodide.

HYDRARGYRI OXIDUM FLAVUM (Yellow Mercuric Oxide).

CHARACTERS.

An orange-yellow, odourless amorphous powder.

Insoluble in water and alcohol.

USES.

Antiseptic. Used as an ointment or lotion for treatment of venereal sores, and as an oculentum in conjunctivitis.

PREPARATIONS.

Lotio Hydrargyri Flavum, B.P.C. (Lot. Hydrarg. Flav.).—Yellow Mercurial Lotion. *Syn.*—Yellow Wash. It contains freshly precipitated mercuric oxide, prepared from solution of calcium hydroxide and about 0·5% w/v of mercuric chloride.

Oculentum Atropinæ cum Hydrargyri Oxido, B.P. (Oculent. Atrop. c. Hydrarg. Oxid.).—Atropine and Yellow Mercuric Ointment for the Eye. Atropine sulphate, 0·125%, and yellow mercuric oxide, 1%, in simple eye ointment. It should be stored in small, well-closed containers in a cool place and protected from light.

Oculentum Hydrargyri Oxidi, B.P. (Oculent. Hydrarg. Oxid.).—Yellow Mercuric Oxide Ointment for the Eye. Yellow mercuric oxide, 1%, in simple eye ointment. It should be stored in small, well-closed containers in a cool place and protected from light.

Unguentum Hydrargyri Flavi, B.P.C. (Ung. Hydrarg. Flav.).—Yellow Mercuric Oxide Ointment. Yellow mercuric oxide, 2%, with liquid paraffin, in yellow soft paraffin.

HYDRARGYRI OXYCYANIDUM (Mercury Oxycyanide).

CHARACTERS.

A white, crystalline powder.

Soluble 1 in about 18 parts of water.

USES.

A powerful antiseptic. Antisyphilitic.

DISPENSING.

Solutions for injection may be prepared by aseptic methods.

DOSE.

By intramuscular injection, $\frac{1}{12}$ to $\frac{1}{6}$ gr. (0·005 to 0·01 gm.); by intravenous injection $\frac{1}{6}$ gr. (0·01 gm.).

PREPARATION.

Solvellæ Hydrargyri Oxycyanidi, B.P.C. (Solv. Hydrarg. Oxycyanid.).—Mercuric Oxycyanide Solution Tablets. Each tablet contains nearly $4\frac{1}{2}$ gr. of mercuric oxycyanide coloured with eosin. One tablet dissolved in 20 fl. ozs. of water forms a solution containing 1 in 2000 of mercuric oxycyanide.

HYDRARGYRI PERCHLORIDUM (Mercuric Chloride).

SYNONYMS.

Corrosive Sublimate; Perchloride of Mercury.

CHARACTERS.

A heavy white crystalline powder, or white crystalline masses.

Soluble 1 in 18 parts of water, and 1 in 4 parts of alcohol (90%).

USES.

Powerful antiseptic. Antisyphilitic.

DISPENSING.

Often prescribed with potassium iodide, when red mercuric iodide is formed, which redissolves in the presence of excess of the potassium salt.

DOSE.

$\frac{1}{32}$ to $\frac{1}{16}$ gr. (0·002 to 0·004 gm.).

PREPARATIONS.

Liquor Hydrargyri Perchloridi, B.P. (Liq. Hydrarg. Perchlor.).—Solution of Mercuric Chloride. An aqueous solution containing 0·1% w/v of mercuric chloride; 1 fl. dr. contains about $\frac{1}{16}$ gr., and 4 mils contains 0·004 gm., of mercuric chloride.

It should be stored protected from light. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

Solvellæ Hydrargyri Perchloridi, B.P.C. (Solv. Hydrarg Perchlor.).—Mercuric Chloride Solution Tablets. *Syn.*—Antiseptic Perchloride Tablets; Antiseptic Corrosive Sublimate Tablets. Each tablet contains 8¾ gr. of mercuric chloride with sodium chloride and methylene blue. One tablet dissolved in 20 fl. ozs. of water forms a solution containing 1 in 1000 of mercuric chloride.

HYDRARGYRI SUBCHLORIDUM (Mercurous Chloride).

SYNONYMS.

Calomel; Subchloride of Mercury.

CHARACTERS.

A dull, white, heavy powder, becoming yellow when triturated or compressed.

USES.

Purgative and antisyphilitic.

DISPENSING.

When given as a purgative at night, a saline purgative is often given before breakfast the following morning to minimize adsorption of mercury.

DOSE.

½ to 3 gr. (0·03 to 0·2 gm.); by intramuscular injection, ½ to 1 gr. (0·03 to 0·06 gm.); for a child 1 year old, 1 gr.

PREPARATIONS.

Injectio Hydrargyri Subchloridi, B.P.—Injection of Mercurous Chloride, 5% w/v $HgCl_2$. *Syn.*—Calomel Injection. A sterile oily suspension of calomel, in olive oil and wool fat, and containing camphor and creosote. For use as an intramuscular injection. *Dose*—By intramuscular injection, 10 to 20 min. (0·6 to 1·2 mil).

Lotio Hydrargyri Nigra, B.P.—Black Mercurial Lotion, 0·7%. *Syn.*—Black Wash. Prepared by triturating mercurous chloride with glycerin, and adding in portions solution of calcium hydroxide.

Pilulæ Hydrargyri Subchloridi Compositæ, B.P.C. (Pil. Hydrarg. Subchlor. Co.).—Compound Mercurous Chloride Pills. *Syn.*—Compound Calomel Pills; Plummer's Pill. Each

pill contains 1 gr. of mercurous chloride, 1 gr. of sulphurated antimony and 2 gr. of guaiacum resin. *Dose*—1 or 2 pills.

Unguentum Hydrargyri Subchloridi, B.P. (20%).—*Syn.* —Calomel Ointment. A white ointment, prepared by mixing mercurous chloride (calomel) and simple ointment.

HYDRARGYRI AMMONIATUM (Ammoniated Mercury).

SYNONYM.

White Precipitate.

CHARACTERS.

A white odourless powder.

Insoluble in water, alcohol and ether.

USES.

A stimulant in chronic skin diseases and to destroy pediculi.

PREPARATIONS.

Unguentum Hydrargyri Ammoniati, B.P. (Ung. Hydrarg. Ammon.).—Ointment of Ammoniated Mercury. *Syn.*—Ammoniated Mercury Ointment; White Precipitate Ointment. Ammoniated mercury, 5%, in simple ointment.

Unguentum Hydrargyri Ammoniati Dilutum, B.P.C. (Ung. Hydrarg. Ammon. Dil.).—Dilute Ammoniated Mercury Ointment. Ointment of ammoniated mercury and simple ointment, equal parts.

HYDRARGYRUM OLEATUM (Oleated Mercury).

CHARACTERS.

A light yellow unctuous substance.

USES.

In the form of Unguentum Hydrargyri Oleati for syphilitic lesions and chronic skin diseases.

PREPARATION.

Unguentum Hydrargyri Oleati, B.P. (Ung. Hydrarg. Oleat.).—Ointment of Oleated Mercury. *Syn.*—Mercuric Oleate Ointment. Oleated mercury, 25%, in simple mercury.

HYDROGENII PEROXIDI, LIQUOR (10 volumes).

CHARACTERS.

A colourless, odourless aqueous solution of hydrogen peroxide.

STORAGE.

In neutral glass containers, closed with a glass stopper, in a cool place, and protected from light.

USES.

Antiseptic. It is used to cleanse wounds.

DOSE.

½ to 2 fl. dr. (2 to 8 mils).

NOTE.—The 10-volume solution is equivalent to 3% strength.

HYOSCYAMUS (Hyoscyamus).

SYNONYMS.

Hyoscyami Folia, Henbane Leaves.

The dried leaves and flowering tops of *Hyoscyamus niger* Linn.

CONSTITUENTS.

Contains the alkaloid hyoscyamine, with hyoscine and atropine. Should contain not less than 0·05% alkaloids calculated as hyoscyamine.

USES.

Narcotic, anodyne, sedative. Used to counteract the griping action of purgatives, such as calomel or aloes.

DOSE.

3 to 6 gr. (0·2 to 0·4 gm.).

PREPARATIONS.

Extractum Hyoscyami Liquidum, B.P. (Ext. Hyoscy. Liq.).—Liquid Extract of Hyoscyamus. It is prepared with alcohol (70%), concentration being effected under reduced pressure at a temperature not exceeding 60°. It is adjusted to contain 0·05% w/v of the alkaloids of hyoscyamus, calculated as hyoscyamine; 6 min. contains about $\frac{1}{370}$ gr., and 0·4 mil contains 0·0002 gm., of alkaloids. *Dose*—3 to 6 min. (0·2 to 0·4 mil).

Extractum Hyoscyami Siccum, B.P. (Ext. Hyoscy. Sicc.).—Dry Extract of Hyoscyamus. It is prepared with alcohol (70%) and adjusted with hyoscyamus, in fine powder, to contain 0·3% of the alkaloids of hyoscyamus, calculated as hyoscyamine; 1 gr. contains about $\frac{1}{350}$ gr., and 0·06 gm. contains 0·00018, of alkaloids. It should be stored in small, wide-mouthed, well-closed containers in a cool place. *Dose*—$\frac{1}{4}$ to 1 gr. (0·016 to 0·06 gm.).

Pilula Colocynthidis et Hyoscyami, B.P. (Pil. Colocynth. et Hyoscy.).—Pill of Colocynth and Hyoscyamus. Colocynth, about 12·5%, aloes and scammony resin, of each about 25%, with curd soap, oil of clove, dry extract of hyoscyamus and syrup of liquid glucose. *Dose*—4 to 8 gr. (0·25 to 0·5 gm.).

Tinctura Hyoscyami, B.P. (Tinct. Hyoscy.).—Tincture of Hyoscyamus. Liquid extract of hyoscyamus, 10%, v/v, in alcohol (70%). It contains 0·005% w/v of the alkaloids of hyoscyamus, calculated as hyoscyamine; 1 fl. dr. contains about $\frac{1}{370}$ gr., and 4 mils contains 0·0002 gm., of alkaloids. *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

HYOSCINÆ HYDROBROMIDUM (Hyoscine Hydrobromide).

SYNONYM.

Scopolamine Hydrobromide.

CHARACTERS.

Colourless, odourless crystals.

Soluble 1 in about 2 parts of water, and 1 in 13 parts of alcohol (90%).

USES.

Powerful hypnotic.

DISPENSING.

Generally administered hypodermically. Solutions for injection may be sterilized by heating with a bactericide or filtration, and containers must comply with the limit test for alkalinity of glass.

DOSE.

$\frac{1}{200}$ to $\frac{1}{100}$ gr. (0·0003 to 0·0006 gm.).

PREPARATION.

Oculentum Hyoscinæ, B.P. (Oculent. Hyoscin.).—Hyoscine Ointment for the Eye. Hyoscine Hydrobromide, 0·125%, in simple eye ointment. It should be stored in small, well-closed containers in a cool place and protected from light.

ICHTHAMMOL (Ichthammol).

SYNONYMS AND PROPRIETARY NAMES.

Ammonium Ichthyosulphonate; Ichthyol (*Österreichische Ichthyol-Gesellschaft, Seefeld im Tyrol; Martindale, London*); Isarol (*Ciba, London*); Perichthol (*British Drug Houses, London*); Subitol (*C. Zimmerman, London*).

CHARACTERS.

A black viscous liquid with a strong characteristic odour. *Soluble* in water, partially soluble in alcohol (90%), *miscible* with oils and glycerin.

USES.

For treatment of skin diseases and as an intestinal antiseptic.

DISPENSING.

For internal use ichthammol is dispensed in pills or capsules. Externally it is applied as an aqueous lotion, glycerin paint, or in ointments. It can be incorporated in a calamine, zinc oxide, lime-water cream for application to skin diseases. It is also applied in pessaries or suppositories.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

PREPARATIONS.

Gelatinum Zinci et Ichthammolis, B.P.C. (Gelat. Zinc. et Ichtham.).—Gelatin of Zinc and Ichthammol. *Syn.*—Pasta Zinci et Ichthammolis; Unna's Paste with Ichthammol. Ichthammol, about 2%, with zinc oxide, glycerin, gelatin and distilled water.

Glycerinum Ichthammolis, B.P.C. (Glycer. Ichtham.).—Glycerin of Ichthammol. *Syn.*—Glycerin of Ammonium Ichthosulphonate, 1 in 10.

Unguentum Ichthammolis, B.P.C. (Ung. Ichtham.).—Ichthammol Ointment. *Syn.*—Ammonium Ichthyosulphonate Ointment. Ichthammol, 10%, in wool fat ointment.

INDICARMINUM (Indigo Carmine).

SYNONYM.

Sodium Indigotin disulphonate.

CHARACTERS.

Odourless blue powder or granules with a coppery lustre and saline taste.

USES.

Employed as a test for renal efficiency.

DISPENSING.

Solutions for injection may be sterilized by heating in an autoclave or by filtration. Solutions should be protected from light.

DOSE.

By intra-muscular injection, $\frac{3}{4}$ to $1\frac{1}{2}$ gr. (0·05 to 0·1 gm.); by intravenous injection $\frac{1}{8}$ to $\frac{1}{4}$ gr. (0·008 to 0·016 gm.).

INSULINUM (Insulin).

A preparation containing the specific antidiabetic principle of the mammalian pancreas. Prepared from pancreas which is either fresh or which has been kept frozen from the time of removal from the body. The principle is isolated as a hydrochloride in powder form and may be compounded as follows:

(*a*) *In Solution.*—Insulin solution is prepared by dissolving the necessary amount of the powder in distilled water which has been acidified to a reaction between *p*H 3 and *p*H 4, so that the solution contains 20 units per mil. A small quantity of some antiseptic such as phenol is usually added, and the solution sterilized by filtration. If it is placed in ampoules, each of which contains one dose only, no antiseptic is necessary. The solution must be stored so that the temperature does not exceed 20°, and the solution must not be used after 18 months of its manufacture.

(*b*) *In Tablet Form.*—Insulin tablets are made by mixing the powder with lactose and compressing into tablets, which must be sterile and packed in sterile containers. The label must state the number of units in each tablet. *Dose*—By subcutaneous injection 5 to 100 units.

PREPARATION.

Protamine Insulate.—*Syn.* and *Prop. Name*—Protamine Insulin, Insulin-P, Delay Insulin. A compound of insulin with a protamine. Protamine Zinc Insulin—(Zinc Protamine Insulin), prepared by adding traces of zinc to protamine insulin. Both these preparations have a more prolonged action than Insulin.

IODOFORMUM (Iodoform).

CHARACTERS.

Shining lemon-yellow crystalline scales, with a persistent penetrating odour.

Soluble only slightly in water, 1 part in 100 of alcohol 90%), 1 part in 8 of ether, and 1 part in about 100 of glycerin.

USES.

Antiseptic.

DOSE.

½ to 3 gr. (0·03 to 0·2 gm.).

PREPARATIONS.

Glycerinum Iodoformi, B.P. (Glycer. Iodof.).—Glycerin of Iodoform. *Syn.*—Emulsio Iodoformi. 1 in 10.

Oculentum Iodoformi, B.P. (Oculent. Iodof.).—Iodoform Ointment for the Eye. Iodoform, 4%, in simple eye ointment. It should be stored in small, well-closed containers in a cool place, and protected from light.

Pasta Bismuthi et Iodoformi, B.P.C. (Past. Bism. et Iodof.) —Bismuth and Iodoform Paste. *Syn.*—B.I.P.P. Bismuth subnitrate, 25%, and iodoform, 50%, with liquid paraffin.

Pasta Zinci et Iodoformi.—Zinc and Iodoform Paste. *Syn.*—Z.I.P.P. Used, as B.I.P.P., as a paste applied to wounds and ulcers to control sepsis. Z.I.P.P. is said to be less toxic. It is cheaper than B.I.P.P.

IODOPHTHALEINUM (Iodophthaleinum).

SYNONYMS AND PROPRIETARY NAMES.

Sodium Tetriodophenolphthalein, Iodo-Ray (*Martindale, London*); Iod-Tetragnost (*Merck, Darmstadt; Martindale, London*); Opacin (*May & Baker, London*); Stipulæ (*Burroughs Wellcome, London*).

CHARACTERS.

A blue crystalline powder.

Soluble 1 in about 7 parts of water.

USES.

Renders the gall bladder opaque to X-rays.

DISPENSING.

Solutions for injection may be sterilized by tyndallization or filtration, and the containers should comply with the tests for limit of alkalinity of glass.

DOSE.

$\frac{1}{3}$ to $\frac{1}{2}$ gr. per pound body weight up to 75 gr. (0·04 to 0·06 gm. per kilogramme body weight up to 5 gm.). By intravenous injection up to 45 gr. (3 gm.).

IODOXYLUM (Iodoxyl).

SYNONYMS AND PROPRIETARY NAMES.

Pyelectan (*Glaxo, London*), Pylumbrin (*Boots, Nottingham*), Uropac (*Pharmaceutical Specialities, May & Baker, London*), Uroselectan B (*Schering, London*).

CHARACTERS.

A white odourless powder.

Soluble, 1 in 1·2 parts of water, and 1 in 100 of alcohol.

Insoluble in ether, and chloroform.

USES.

Injected intravenously to render urinary tract opaque to X-rays.

DISPENSING.

Solutions for injection are sterilized by filtration.

DOSE.

150 to 225 gr. (10 to 15 gm.), by intravenous injection.

IODUM (Iodine).

CHARACTERS.

Heavy brittle laminar crystals, with penetrating odour and acrid taste.

Soluble only slightly in water, 1 part in 12 of alcohol, 1 part

in 65 of glycerin. Very soluble in concentrated aqueous potassium iodide solution.

USES.

Internally, iodine as Liquor Iodi Simplex is administered in milk for chronic rheumatism. Externally iodine is applied as a counter irritant, and antiseptic.

PREPARATIONS.

Liquor Iodi Fortis, B.P. (Liq. Iod. Fort.).—Strong Solution of Iodine. *Syn.*—Tincture Iodi Fortis; Strong Tincture of Iodine. It contains 10% w/v of iodine and 6% w/v of potassium iodide in distilled water and alcohol (90%). It should be stored in well-closed, glass-stoppered bottles.

Liquor Iodi Mitis, B.P. (Liq. Iod. Mit.).—Weak Solution of Iodine. *Syn.*—Tincture Iodi Mitis; Weak Tincture of Iodine; Tinctura Iodi; Tincture of Iodine. It contains 2·5% w/v of iodine and 1·5% w/v of potassium iodide in distilled water and alcohol (90%). 30 min. contains about $\frac{4}{5}$ gr. of free iodine and about 1 gr. of total iodine; 2 mils contains 0·05 gm. of free iodine and about 0·07 gm. of total iodine. It should be stored in well-closed, glass-stoppered bottles.

Liquor Iodi Oleosus, B.P.C. (Liq. Iod. Oleos.).—Oily Solution of Iodine. *Syn.*—Tincture Iodi Oleosa; Oily Tincture of Iodine. Iodine, 8% w/v, and castor oil, 16·25% v/v, in alcohol (90%).

Liquor Iodi Simplex, B.P. (Liq. Iod. Simp.).—Simple Solution of Iodine. A solution containing 9% w/v of total iodine in alcohol (95%), corresponding approximately to 10% w/w of total iodine. 15 min. contains about $1\frac{1}{2}$ gr., and 1 mil contains 0·09 gm., of total iodine. It is of the same strength as Tinctura Iodi (French Codex, 1908). It should be stored in well-closed bottles, in a cool place and protected from light. When stored, the proportion of free iodine decreases owing to interaction with the alcohol. *Dose*—3 to 15 min. (0·2 to 1 mil).

Unguentum Iodi Denigrescens, B.P.C. (Ung. Iod. Denig.).—Non-Staining Iodine Ointment. Iodine, 5%, with arachis oil and yellow soft paraffin.

IPECACUANHA (Ipecacuanha).

The dried root of *Cephælis Ipecacuanha* (Brot.) A. Rich.

CONSTITUENTS.

Emetine and cephæline and a smaller quantity of psycho

trine. It should contain not less than 2 per cent. of total alkaloids calculated as emetine, of which not less than three-fifths consists of non-phenolic alkaloids calculated as emetine.

USES.

In small doses as an expectorant, and in large doses as an emetic.

PREPARATIONS.

Extractum Ipecacuanhæ Liquidum, B.P. (Ext. Ipecac. Liq.).—Liquid Extract of Ipecacuanha. It is prepared with alcohol (90%), concentration being effected under reduced pressure at a temperature not exceeding 60°. It is adjusted to contain 2% w/v of the total alkaloids of ipecacuanha, calculated as emetine; 2 min. contains about $\frac{1}{25}$ gr., and 0·12 mil contains about 0·0024 gm., of the total alkaloids of ipecacuanha, calculated as emetine. *Dose*—$\frac{1}{2}$ to 2 min. (0·03 to 0·12 mil). *Emetic dose*—10 to 30 min. (0·6 to 2 mils).

Ipecacuanha Pulverata, B.P. (Ipecac. Pulverat.).—Powdered Ipecacuanha. *Syn.*—Powdered Ipecacuanha Root; Pulvis Ipecacuanhæ. Ipecacuanha, reduced to a fine powder and adjusted with lactose, or with ipecacuanha of suitable alkaloidal content, to contain 2% of the total alkaloids of ipecacuanha, calculated as emetine, of which not less than two-thirds consists of the non-phenolic alkaloids, calculated as emetine. 2 gr. contains about $\frac{1}{25}$ gr., and 0·12 gm. contains 0·0024 gm., of the total alkaloids of ipecacuanha, calculated as emetine. Ash, not more than 5·5%. It should be stored in well-closed containers. *Dose*—$\frac{1}{2}$ to 2 gr. (0·03 to 0·12 gm.). *Emetic dose*—15 to 30 gr. (1 to 2 gm.).

Mistura Ipecacuanhæ Composita, B.P.C. (Mist. Ipecac. Co.).—Compound Ipecacuanha Mixture. *Syn.*—Mistura Expectorans. Each fluid ounce contains 24 min. of vinegar of ipecacuanha, 15 min. of strong solution of ammonium acetate and 15 min. of oxymel of squill, with glycerin and chloroform water. *Dose*—$\frac{1}{2}$ to 1 fl. oz. (15 to 30 mils).

Pulvis Ipecacuanhæ et Opii, B.P. (Pulv. Ipecac. et Opii).—Powder of Ipecacuanha and Opium. *Syn.*—Pulvis Opii et Ipecacuanhæ Compositus I.A.; Pulvis Ipecacuanhæ Compositus; Compound Powder of Ipecacuanha; Dover's Powder. Powdered ipecacuanha and powdered opium, of each 10%, with lactose. It contains 1% of anhydrous morphine; 10 gr. contains $\frac{1}{10}$ gr., and 0·6 gm. contains 0·006 gm., of anhydrous morphine. *Dose*—5 to 10 gr. (0·3 to 0·6 gm.).

Tabellæ Acidi Acetylsalicylici et Opii Compositæ, B.P.C. (Tab. Acid. Acetylsalicyl. et Opii).—Compound Tablets of

Acetylsalicylic Acid and Opium. Each tablet contains 3 gr. of acetylsalicylic acid, $1\frac{1}{4}$ gr. of phenacetin and 1 gr. of powder of ipecacuanha and opium. *Dose*—1 to 4 tablets.

Tabellæ Aloini Compositæ, B.P.C. (Tabl. Aloin. Co.).—Compound Aloin Tablets. Each tablet contains $\frac{1}{5}$ gr. of aloin, $\frac{1}{4}$ gr. of ipecacuanha and $\frac{1}{8}$ gr. of dry extract of nux vomica. *Dose*—1 or 2 tablets.

Tinctura Ipecacuanhæ, B.P. (Tinct. Ipecac.)—Tincture of Ipecacuanha. Liquid extract of ipecacuanha, 5% v/v, in alcohol (90%), glycerin and distilled water. It contains 0·1% w/v of the total alkaloids of ipecacuanha, calculated as emetine; 30 min. contains about $\frac{1}{37}$ gr., and 2 mils contains 0·002 gm., of alkaloid. Tincture of ipecacuanha replaces Vinum Ipecacuanhæ, Ipecacuanha Wine, of the British Pharmacopœia, 1914, and contains the same proportion of liquid extract. When Vinum Ipecacuanhæ or Ipecacuanha Wine is prescribed or demanded, Tinctura Ipecacuanhæ must be dispensed or supplied. *Dose*—10 to 30 min. (0·6 to 2 mils). *Emetic dose*—$\frac{1}{2}$ to 1 fl. oz. (15 to 30 mils).

Trochiscus Morphinæ et Ipecacuanhæ, B.P. (Troch. Morph. et Ipecac.).—Lozenge of Morphine and Ipecacuanha. *Syn.*—Morphine and Ipecacuanha Lozenge. Each Lozenge contains approximately $\frac{1}{32}$ gr. or 0·002 gm. of morphine hydrochloride and approximately $\frac{1}{10}$ gr. or 0·006 gm. of powdered ipecacuanha.

IPOMŒA (Ipomœa).

SYNONYMS.

Ipomœæ Radix, Orizaba Jalap Root, Mexican Scammony Root.

The dried root of *Ipomœa orizabensis* (Peller.) Ledanois.

USES.

Drastic purgative, the source of scammony resin, in which form it is usually administered.

DOSE.

5 to 20 gr. (0·3 to 1·2 gm.).

JALAPA (Jalap).

The dried tubercles of *Ipomœa purga* Hayne.

USES.

A drastic purgative.

DISPENSING.

When jalap is prescribed, Jalapa Pulverata, the standardized powder, should be dispensed.

PREPARATIONS.

Jalapa Pulverata, B.P. (Jalap. Pulverat.).—Powdered Jalap. *Syn.*—Pulvis Jalapæ. Jalap, reduced to a fine powder and adjusted with powdered exhausted jalap or lactose to contain 10% of resin. Ash, not more than 6·5%. It should be stored in well-closed containers. *Dose*—5 to 20 gr. (0·3 to 1·2 gm.).

Pulvis Jalapæ Compositus, B.P. (Pulv. Jalap. Co.).—Compound Powder of Jalap. Powdered jalap, 30%, with potassium acid tartrate and ginger. *Dose*—10 to 60 gr. (0·6 to 4 gm.).

Tinctura Jalapæ (Tinct. Jalap.).—Tincture of Jalap. It contains from 1·45% to 1·55% w/v of resin. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

KAOLINUM (Kaolin).

CHARACTERS.

A soft whitish powder.
Insoluble in water.

USES.

For adsorbing toxins in the alimentary canal, when it is administered in suspension in water. Also used in the preparation of Cataplasma Kaolin.

DOSE

½ to 2 oz. (15 to 60 gm.).

PREPARATIONS.

Cataplasma Kaolini, B.P. (Cataplasm. Kaolin.).—Poultice of Kaolin. It contains approximately 53% w/w of kaolin, with boric acid, methyl salicylate, oil of peppermint, thymol and glycerin.

Emulsio Paraffini Liquidi et Kaolini, B.P.C. (Emuls. Paraff. Liq. et Kaolin.).—Emulsion of Liquid Paraffin and Kaolin. Each fluid ounce contains 2 fl. dr. of liquid paraffin and about 80 gr. of kaolin. *Dose*—½ to 2 fl. ozs. (15 to 60 mils).

KINO (Kino).

The dried juice obtained from the trunk of *Pterocarpus Marsupium* Roxb.

USES.

A powerful astringent. Employed in mouth washes or gargles in the form of the diluted tincture; as a lozenge; and as Pulvis Kino Compositus for diarrhœa.

DOSE.

5 to 20 gr. (0·2 to 1·2 gm.).

PREPARATIONS.

Pulvis Kino Compositus, B.P.C. (Pulv. Kino. Co.).—Compound Powder of Kino. Kino, 75%, powdered opium, 5%, and cinnamon, 20%. *Dose*—5 to 20 gr. (0·3 to 1·2 gm.).

Tinctura Kino, B.P.C. (Tinct. Kino).—Tincture of Kino. 1 in 10. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

KRAMERIA (Krameria).

The dried root of *Krameria triandra* Ruiz et Pav.

USES.

A powerful astringent.

DOSE.

10 to 30 gr. (0·6 to 2 gm.).

PREPARATIONS.

Extractum Krameriæ Siccum, B.P. (Ext. Kramer. Sicc.).—Dry Extract of Krameria. It is prepared with water and evaporated to dryness under reduced pressure. It should be stored in small, wide-mouthed, well-closed containers in a cool place. *Dose*—5 to 15 gr. (0·3 to 1 gm.).

Tinctura Krameriæ, B.P. (Tinct. Kramer.).—Tincture of Krameria. 1 in 5, by percolation with alcohol (60%). *Dose*—½ to 1 fl. dr. (2 to 4 mils).

Trochiscus Krameriæ, B.P. (Troch. Kramer.).—Lozenge of Krameria. *Syn.*—Krameria Lozenge. Each lozenge contains approximately 1 gr. or 0·06 gm. of dry extract of krameria.

Trochiscus Krameriæ et Cocainæ, B.P. (Troch. Kramer. et Cocain.).—Lozenge of Krameria and Cocaine. *Syn.*—

Krameria and Cocaine Lozenge. Each lozenge contains approximately 1 gr. or 0·06 gm. of dry extract of krameria and approximately $\frac{1}{20}$ gr. or 0·003 gm. of cocaine hydrochloride.

LEPTAZOLUM (Leptazol).

SYNONYM.

Metrazol, formerly sold as "Cardiazol."

CHARACTERS.

Colourless crystals, or crystalline powder, taste bitter. *Soluble*, readily in water, alcohol, ether, and chloroform.

USES.

Powerful respiratory and cardiac stimulant. Also used as a convulsant in schizophrenia.

DOSE.

$\frac{3}{4}$ to $1\frac{1}{2}$ gr. (0·05 to 0·1 gm.).

PREPARATION.

Injectio Leptazoli (Injection of Leptazol).—Leptazol 10%, with sodium phosphate, 0·25%, in distilled water. Adjust to *p*H 7·8 with Hydrochloric Acid or Sodium Hydroxide. An antiseptic must *not* be added to multiple dose containers. Sterilize by autoclaving or by filtration. *Dose*—By subcutaneous injection, 8 to 15 min. (0·5 to 1·0 mil). By intravenous injection, as a convulsant, 30 to 75 min., increasing to 180 min. (2·0 to 5·0 mil, increasing to 12·0 mil).

LIMONIS CORTEX (Lemon Peel).

The outer part of the fresh pericarp of Citrus Limonia Osbec.

USES.

Aromatic. Flavouring agent.

PREPARATIONS.

Syrupus Limonis, B.P. (Syr. Limon.).—Syrup of Lemon. It contains the alcohol-soluble matter of 6% w/v of lemon peel with citric acid and syrup. It should be stored in a cool place in a container previously washed with boiling water. *Dose*—$\frac{1}{2}$ to 2 fl. dr. (2 to 8 mils).

Tinctura Limonis, B.P. (Tinct. Limon.).—Tincture of Lemon. 1 in 4, by maceration with alcohol (60%). *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

LINUM (Linseed).

The dried ripe seeds of *Linum usitatissimum* Linn.

USES.

Demulcent and emollient (Infusion of Linseed, for cough).

PREPARATIONS.

Infusum Lini, B.P.C. (Inf. Lini).—Infusion of Linseed. About 1 in 30. *Dose*—1 to 4 fl. ozs. (30 to 120 mils).

Linum Contusum, B.P. (Linum Contus.).—Crushed Linseed. *Syn.*—Lini Semina Contusa ; Linseed Meal. Linseed, coarsely powdered, containing not less than 30% of fixed oil, and exhibiting only an occasional starch grain in the residue. Ash, not more than 5%. It should be recently prepared.

LOBELIA (Lobelia).

SYNONYM.

Indian Tobacco.

The dried aerial parts of *Lobelia inflata* Linn.

CONSTITUENT.

Lobeline, an alkaloid.

USES.

Powerful respiratory stimulant. Antispasmodic in asthma.

DOSE.

1 to 3 gr. (0·06 to 0·2 gm.).

PREPARATIONS.

Lobelinum Hydrochloricum.—White crystals, *soluble* 1 in 50 of water ; solutions must not be heated. *Dose*—By intravenous injection, as respiratory stimulant, $\frac{1}{6}$ gr. (0·01 gm.) in 1% solution.

Mistura Lobeliæ et Stramonii Composita, B.P.C. (Mist. Lobel. et Stramon. Co.).—Compound Mixture of Lobelia and Stramonium. Each fluid ounce contains 4 gr. of ammonium carbonate, 5 gr. of potassium iodide and 10 min. each of ethereal tincture of lobelia and tincture of stramonium, in chloroform water. *Dose*—$\frac{1}{2}$ to 1 fl. oz. (15 to 30 mils).

Pulvis Lobeliæ Compositus, B.P.C. (Pulv. Lobel. Co.).—Compound Lobelia Powder. Equal parts of lobelia, stramonium and tea, impregnated with potassium nitrate and oil of anise.

Pulvis Stramonii Compositus, B.P.C. (Pulv. Stramon. Co.).—Compound Stramonium Powder. Stramonium, 1 in 2, with lobelia, anise and tea, impregnated with potassium nitrate and oil of eucalyptus.

Tinctura Lobeliæ Ætherea, B.P. (Tinct. Lobel. Æther.).—Ethereal Tincture of Lobelia. 1 in 5, by percolation with spirit of ether. *Dose*—5 to 15 min. (0·3 to 1 mil).

MAGNESII CARBONAS LEVIS (Light Magnesium Carbonate).

CHARACTERS.

A very light, white, stable powder, which is odourless and tasteless.

Almost *insoluble* in water and alcohol.

USES.

Antacid and laxative.

DISPENSING.

The light variety of magnesium carbonate is usually dispensed in mixture form, or as a powder to be taken in milk. The heavy variety (see below) is used for cachets and powders, since it is weight for weight less in bulk, and therefore more convenient.

DOSE.

10 to 60 gr. (0·6 to 4·0 gm.).

PREPARATIONS.

Mistura Alba, B.P.C. (Mist. Alb.).—White Mixture. Each fluid ounce contains 20 gr. of light magnesium carbonate, and 120 gr. of magnesium sulphate. *Dose*—$\frac{1}{2}$ to 1 fl. oz. (15 to 30 mils).

Magnesii Carbonas Ponderosus.—Heavy Magnesium Carbonate. A white granular powder, similar in action to light magnesium carbonate, but weight for weight smaller in bulk and hence more convenient. *Dose*—10 to 60 gr. (2 to 4 gm.).

Liquor Magnesii Bicarbonatis, B.P. (Liq. Mag. Bicarb.).—Solution of Magnesium Carbonate. *Syn.*—Fluid Magnesia. It contains not less than 2·5% w/v of $Mg(HCO_3)_2$, 2 fl. ozs. contains the equivalent of about 15 gr., and 60 mils contains the equivalent of about 1 gm., of magnesium carbonate. It should be stored in well-closed containers in a cool place. *Dose*—1 to 2 fl. ozs. (30 to 60 mils). See also under Mag. Sulph.

MAGNESII OXIDUM LEVE (Light Magnesium Oxide).

SYNONYMS.
Magnesia Levis ; Light Magnesia.

CHARACTERS.
A light, white, odourless powder.
Almost *insoluble* in water and alcohol.

USES.
Antacid and mild laxative.

DISPENSING.
Administered in powder form or suspended in milk. The light *carbonate* should be prescribed with sodium bicarbonate in mixture form. The heavy variety of oxide (see below) is used for cachets and powders.)

DOSE.
10 to 60 gr. (0·6 to 4·0 gm.).

PREPARATION.
Magnesii Oxidum Ponderosum.—Heavy Magnesium Oxide. *Syn.*—Magnesia Ponderosa ; Heavy Magnesia. A white odourless powder, similar in action to light magnesium oxide, but weight for weight less in bulk and hence more convenient. *Dose*—10 to 60 gr. (0·6 to 4·0 gm.).

MAGNESII SULPHAS (Magnesium Sulphate).

SYNONYM.
Epsom Salts.

CHARACTERS.
Colourless, odourless crystals.
Soluble 1 in 1·5 parts of water.

USES.
Hydragogue. Purgative.

DISPENSING.
Solutions for injection may be sterilized by heating in an autoclave or filtration.

DOSE.
½ to 4 dr. (2 to 16 gm.).

PREPARATIONS.

Magnesii Sulphas Effervescens, B.P.C. (Mag. Sulph. Efferv.).—Effervescent Magnesium Sulphate. *Syn.*—Effervescent Epsom Salts. About 1 in 2 of the crystalline salt. *Dose*—for repeated administration 1 to 3 dr. (4 to 12 gm.). For a single administration ½ to 1 oz. (16 to 30 gm.).

Mistura Alba, B.P.C. (Mist. Alb.).—White Mixture. Each fluid ounce contains 120 gr. of magnesium sulphate and 20 gr. of light magnesium carbonate, in peppermint water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Mistura Sennæ Composita, B.P. (Mist. Senn. Co.).—Compound Mixture of Senna. *Syn.*—Black Draught. Magnesium sulphate or sodium sulphate, 20% w/v, with liquid extract of liquorice, compound tincture of cardamon and aromatic spirit of ammonia, in infusion of senna. *Dose*—1 to 2 fl. oz. (30 to 60 mils).

Pasta Magnesii Sulphatis, B.P.C. (Past. Mag. Sulph.).—Magnesium Sulphate Paste. *Syn.*—Morison's Paste. Exsiccated magnesium sulphate dried at 100°, 45%, and glycerin, with 0·5% of phenol.

Liquor Magnesii Bicarbonatis, B.P. (2·5% w/v).—*Syn.*—Fluid Magnesia. A colourless liquid, prepared by mixing together a solution of magnesium sulphate in water, heated to boiling-point, and a solution of sodium carbonate in water, boiling, washing carefully the precipitated magnesium carbonate, mixing it with distilled water, and passing pure carbonic acid gas, at three atmospheres pressure, through till it is dissolved. *Dose*—1 to 2 fl. ozs. (30 to 60 mils) ; ½ dr. for a child 1 year old (2 fl. ozs. contain the equivalent of about 15 gr. of magnesium carbonate).

Mistura Magnesii Hydroxidi, B.P. (8·25% w/v).—Mixture of Magnesium Hydroxide. *Syn.*—Cream of Magnesia. It is an aqueous suspension of hydrated magnesium oxide, prepared by adding light magnesium oxide to sodium hydroxide dissolved in water and diluting with water. Pour the suspension into magnesium sulphate dissolved in water, stirring continuously. Collect the precipitate on a calico filter, wash free from sulphate and suspend in water to produce the required volume. Antacid. *Dose*—1 to 4 dr. (4 to 16 mils). (½ fl. oz. contains the equivalent of about 12½ gr. of magnesium oxide.)

Mistura Magnesii Hydroxidi et Paraffini Liquidi, B.P.C. (Mist. Mag. Hydrox. et Paraff. Liq.).—Mixture of Magnesium Hydroxide and Liquid Paraffin. Liquid paraffin, 30% v/v, and mixture of magnesium hydroxide, flavoured with vanillin. *Dose*—1 to 4 fl. dr. (4 to 16 mils).

MAGNESII TRISILICAS (Magnesium Trisilicate).

PREPARATION.

May be prepared by interaction between magnesium sulphate and sodium silicate, in solution.

CHARACTERS.

A white powder. *Insoluble* in water.

USES.

Efficient antacid and absorbent.

DOSE.

5 to 30 gr. (0·3 to 2·0 gm.).

MALTI EXTRACTUM (Extract of Malt).

SYNONYM.

Extractum Bynes.

Diamalt (*British Diamalt Co., Sawbridgeworth*); Kepler (*Burroughs Wellcome, London*); and Maltine (*Glaxo Laboratories, Greenford*) are proprietary brands of extract of malt.

CHARACTERS.

An amber-brown viscous liquid with a sweet taste.

USES.

Nutritive and laxative.

DOSE.

1 to 4 dr. (4 to 16 mils).

PREPARATION.

Extractum Malti cum Oleo Morrhuæ, B.P. (Ext. Malt. c. Ol. Morrh.).—Extract of Malt with Cod-liver Oil. Cod-liver Oil, 10% w/w, in extract of malt. It contains approximately 15% v/v of cod-liver oil; 4 fl. dr. contains about 36 min., and 16 mils. contains about 2·5 mils. *Dose*—1 to 4 fl. dr. (4 to 16 mils).

MEL DEPURATUM (Purified Honey).

CHARACTERS.

A yellowish translucent liquid, being honey strained, whilst hot, through wetted flannel, and the S.G. adjusted to 1·36 by water if necessary.

USES.

Demulcent and sweetening agent.

PREPARATIONS.

Mel Boracis, B.P. (10%).—Borax of Honey. Of the consistence of honey, and prepared by rubbing borax with purified honey and glycerin.

Oxymel, B.P.—Oxymel. A thick syrupy liquid, composed of acetic acid and water and purified honey. Expectorant. *Dose*—½ to 2 dr. (2 to 8 mils).

Oxymel Scillæ, B.P. (5% w/v squill).—Oxymel of Squill. Prepared by macerating bruised squill with acetic acid and water for 7 days, pressing, heating to boiling, filtering, and adding purified honey. Oxymel of squill contains active constituents of squill approximately equivalent to 5% w/v of squill. Expectorant. *Dose*—½ to 1 dr. (2 to 4 mils).

MENTHOL (Menthol).

CHARACTERS.

Colourless crystals, with a penetrating odour.

Soluble 5 in 1 part of alcohol (90 per cent.), 1 in 6 parts of liquid paraffin, 1 in 4 parts of olive oil and almost *insoluble* in water and glycerin.

USES.

Carminative; externally as an antiseptic.

DISPENSING.

For inflamed mucous membranes, menthol is supplied in pastilles (throat and nose), or as an inhalant (throat, nose and larynx). Also dissolved in light liquid paraffin as a spray or as a snuff for the nose.

DOSE.

½ to 2 gr. (0·03 to 0·12 gm.).

PREPARATIONS.

Insufflatio Mentholis, B.P.C. (Insuff. Menthol.).—Menthol Insufflation. *Syn.*—Insufflatio Mentholis Composita; Menthol Snuff. Menthol, 1 in 20, with ammonium chloride, boric acid and lycopodium.

Nebula Mentholis et Thymolis Composita, B.P.C. (Neb. Menthol. et Thymol. Co.).—Compound Menthol and Thymol

Spray. Menthol, camphor and phenol, of each 2% w/v, and thymol, 0·2% w/v, in light liquid paraffin.

Pastilli Mentholis et Eucalyptolis, B.P.C. (Pastil. Menthol. et Eucalyp.).—Menthol and Eucalyptus Pastilles. Each pastille contains menthol, $\frac{1}{20}$ gr., and eucalyptol, $\frac{1}{2}$ min.

Pastilli Mentholis et Cocainæ, B.P.C. (Pastil. Menthol. et Cocain.).—Menthol and Cocaine Pastilles. Each pastille contains menthol, $\frac{1}{20}$ gr., and cocaine hydrochloride, $\frac{1}{40}$ gr.

MEPACRINÆ HYDROCHLORIDUM (Mepacrine Hydrochloride).

SYNONYMS AND PROPRIETARY NAMES.

Atebrin (*Bayer Products, London*), Quinacrine (*Pharmaceutical Specialists, May & Baker, London*).

CHARACTERS.

A bright yellow crystalline powder, odourless, taste bitter. *Soluble* in about 30 parts of water.

USES.

A specific for malaria.

DISPENSING.

A solution for injection may be prepared by dissolving in sterile water immediately before use.

DOSE.

$\frac{3}{4}$ to $1\frac{1}{2}$ gr. (0·05 to 0·1 gm.).

PREPARATION.

Mepacrinæ Methanosulphonas (Mepacrine Methanesulphonate).—A yellow crystalline substance, soluble 1 in 3 of water, and 1 in 36 of alcohol. Used as for Mepacrine Hydrochloride, but is more soluble. Injections for intramuscular use are prepared by dissolving in sterile water, immediately before use. *Dose*—$\frac{3}{4}$ to $1\frac{1}{2}$ gr. (0·05 to 0·1 gm.) by intramuscular injection.

MERSALYLUM (Mersalyl).

SYNONYMS AND PROPRIETARY NAMES.

Mercurgan, Salyrgan (*Bayer Products, London*).

CHARACTERS.

A white, deliquescent powder.

Soluble 1 in about 1 part of water.

USES.

Diuretic.

DISPENSING.

Administered usually intravenously as Injectio Mersalyli. Theophylline is included in the injection as it inhibits the decomposition of the mersalyl into toxic products. The injection may be sterilized by heating in an autoclave or by tyndallization.

PREPARATION.

Injectio Mersalyli, B.P.—Mersalyl, 10 gm., theophylline, 5 gm., in freshly distilled water to 100 mils, adjusted to a *p*H of 7·8 with sodium hydroxide, and sterilized by autoclaving at 110° C. for 20 minutes. *Dose*—8 to 30 min. (0·5 to 2·0 mils).

MESULPHENUM (Mesulphen).

PROPRIETARY NAMES.

Sudermo (*Burroughs Wellcome, London*), Mitigal (*Bayer Products, London*).

CHARACTERS.

A yellow oil, soluble in chloroform and acetone.

USES.

As a stimulant and parasiticide in skin diseases by local application.

METHYL SALICYLAS (Methyl Salicylate).

SYNONYM.

Synthetic Oil of Wintergreen.

CHARACTERS.

A colourless, oily liquid, with an aromatic odour.

Miscible with alcohol, and fixed and volatile oils.

USES.

Local anodyne and antirheumatic.

DOSE.

5 to 15 min. (0·3 to 1 mil).

PREPARATIONS.

Linimentum Methylis Salicylatis, B.P.C. (Lin. Methyl Salicyl.).—Liniment of Methyl Salicylate. *Syn.*—Linimentum Betulæ Compositum; Compound Liniment of Birch. Rectified oil of camphor, 1 in 4, with menthol, oil of eycalyptus and methyl salicylate.

Unguentum Methyl Salicylatis, B.P.C. (Ung. Methyl Salicyl.).—Methyl Salicylate Ointment. *Syn.*—Unguentum Methylis Salicylatis Forte; Strong Methyl Salicylate Ointment. Methyl salicylate, 50%, in white beeswax and hydrous wool fat.

Unguentum Methyl Salicylatis Compositum, B.P.C. (Ung. Methyl Salicyl. Co.).—Compound Methyl Salicylate Ointment. *Syn.*—Unguentum Methylis Salicylatis Compositum Forte; Strong Compound Ointment of Methyl Salicylate; Unguentum Betulæ Compositum; Unguentum Analgesicum; Analgesic Balsam. Methyl salicylate, 50%, and menthol, 10%, with eucalyptol and oil of cajuput, in white beeswax and hydrous wool fat.

METHYLSULPHONAL (Methylsulphonal).

PROPRIETARY NAME.

Trional (*Bayer Products, London*).

CHARACTERS.

White crystalline scales or powder.
Soluble 1 in 320 parts of water.

USES.

Hypnotic.

DOSE.

5 to 20 gr. (0·3 to 1·2 gm.).

METHYLTHIONINÆ CHLORIDUM (Methylene Blue).

CHARACTERS.

Dark green crystalline powder with a metallic lustre.
Soluble 1 in 50 parts of water, and in alcohol.

USES.

Internal antiseptic. Injected intramuscularly as a test for renal efficiency.

DOSE.

1 to 5 gr. (0·06 to 0·3 gm.).

MORPHINÆ HYDROCHLORIDUM (Morphine Hydrochloride).

CHARACTERS.

White, fine, silky needles, or crystalline powder with a bitter taste.

Soluble 1 in 25 parts of water and 1 in 50 parts of alcohol

USES.

Anodyne and narcotic.

DISPENSING.

Solutions for injection may be sterilized by heating with a bactericide or filtration, and glass containers should comply with the tests for limit of alkalinity of glass.

DOSE.

$\frac{1}{8}$ to $\frac{1}{3}$ gr. (0·008 to 0·02 gm.).

PREPARATIONS.

Injectio Morphinæ, B.P.C. (Inj. Morph.).—Injection of Morphine. It contains 2·5% w/v of morphine hydrochloride; 10 min. contains about $\frac{1}{4}$ gr., and 0·6 mil contains about 0·015 gm. of morphine hydrochloride. *Dose*—5 to 10 min. (0·3 to 0·6 mils).

Liquor Morphinæ Hydrochloridi, B.P. (Liq. Morph. Hydrochlor.).—Solution of Morphine Hydrochloride. It contains 1% w/v of morphine hydrochloride in dilute hydrochloric acid, alcohol (90%) and distilled water. 30 min. contains about $\frac{1}{4}$ gr., and 2 mils contains about 0·02 gm., of morphine hydrochloride. *Dose*—5 to 30 min. (0·3 to 2·0 mils).

Mistura Chloroformi Composita, B.P.C. (Mist. Chlorof. Co.).—Compound Chloroform Mixture. *Syn.*—Mistura Tussi Sedativa; Mistura Tussi Rubra. Each fluid drachm contains 15 min. of dilute hydrobromic acid and $\frac{1}{20}$ gr. of morphine hydrochloride, with chloroform, solution of bordeaux B, cherry-

laurel water, syrup of tolu and syrup. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

Suppositorium Morphinæ, B.P. (Supp. Morph.).—Morphine Suppository. Each suppository contains ¼ gr. (0·015 gm.) of morphine hydrochloride.

Tinctura Chloroformi et Morphinæ, B.P.C. (Tinct. Chlorof. et Morph.).—Tincture of Chloroform and Morphine. *Syn.*—Chlorodyne; Tinct. Chlorof. et Morph. B.P. 1885. Chloroform, 1 in 8, morphine hydrochloride, about 1 in 450, and dilute hydrocyanic acid, of about 1 in 16, with ether, alcohol (90%), oil of peppermint, liquid extract of liquorice, treacle, and syrup. *Dose*—5 to 10 min. (0·3 to 0·6 mils).

Tinctura Chloroformi et Morphinæ Composita, B.P.C. (Tinct. Chlorof. et Morph. Co.).—Compound Tincture of Chloroform and Morphine. Chloroform, about 1 in 13, morphine hydrochloride, 1 in 100, with dilute hydrocyanic acid, about 1 in 20, tincture of capsicum, tincture of cannabis, oil of peppermint, glycerin and alcohol (90%). *Dose*—5 to 15 min. (0·3 to 1 mil).

Trochiscus Morphinæ et Ipecacuanhæ, B.P. (Troch. Morph. et Ipecac.).—Lozenge of Morphine and Ipecacuanha. *Syn.*—Morphine and Ipecacuanha Lozenge. Each lozenge contains approximately $\frac{1}{32}$ gr. or 0·002 gm. of morphine hydrochloride and approximately $\frac{1}{10}$ gr. or 0·006 gm. of powdered ipecacuanha.

MORPINÆ SULPHAS (Morphine Sulphate).

CHARACTERS.

White crystal or crystalline powder, odourless, taste bitter. *Soluble*, 1 in 15·5 of water, and 1 in 565 of alcohol, *insoluble* in ether and chloroform.

USES.

Narcotic.

DISPENSING.

Sterilized by heating with a bactericide or by filtration. Containers comply with the tests for limit of alkalinity of glass.

DOSE.

⅛ to ⅓ gr. (0·008 to 0·02 gm.).

MORPHINÆ TARTRAS (Morphine Tartrate).

CHARACTERS.

White needle crystals, or crystalline powder.

Soluble 1 in 11 parts of water.

USES.

Anodyne and narcotic.

DISPENSING.

Solutions for injection may be sterilized by heating with a bactericide or filtration. Glass containers must comply with the limit test for alkalinity of glass.

DOSE.

$\frac{1}{8}$ to $\frac{1}{3}$ gr. (0·008 to 0·02 gm.).

MYRRHA (Myrrh).

An oleo-gum resin obtained from the stem of *Commiphora molmol* Eng., and probably other species.

USES.

Used as a local application (gargle) for relaxed throats, etc., often with borax.

Internally, it is a carminative.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

PREPARATIONS.

Pilulæ Aloes et Myrrhæ, B.P.C. (Pil. Aloes et Myrrh.).—Aloes and Myrrh Pills. *Syn.*—Pilulæ Rufi; Rufus Pills. Each pill contains 2 gr. of aloes and 1 gr. of myrrh. *Dose*—1 or 2 pills.

Tinctura Myrrhæ, B.P. (Tinct. Myrrh.).—Tincture of Myrrh. 1 in 5, by maceration with alcohol (90%). *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

Tinctura Myrrhæ et Boracis, B.P.C. (Tinct. Myrrh et Borac.).—Tincture of Myrrh and Borax. Tincture of myrrh, about 1 in 3, with tincture of krameria, oils of bergamot, lemon, orange, neroli and rosemary, and borax.

NEOARSPHENAMINA (Neoarsphenamine).

SYNONYMS AND PROPRIETARY NAMES.

"914," N.A.B., Novarsphenobenzene, Neo-Kharsivan (*Burroughs Wellcome, London*); Neosalvarsan (*Bayer Products, London*); Novarsenobillon (*May & Baker, London*); Novarson (*Synthetic Drug Co., Toronto; Allen & Hanburys, London*); Novostab (*Boots, Nottingham*).

CHARACTERS.

A yellow, dry, odourless powder.

Soluble in water.

USES.

Antisyphilitic.

DISPENSING.

It is dispensed in sealed glass phials from which the air has been removed and replaced by an inert gas. Solutions for injection are prepared by dissolving the contents of a sealed glass container in the requisite amounts of sterile water. Injections should be made immediately after solution is effected.

DOSE.

By intravenous injection, $2\frac{1}{2}$ to 14 gr. (0·15 to 0·9 gm.).

NIKETHAMIDUM (Nikethamide).

SYNONYMS AND PROPRIETARY NAMES.

N-Diethylnicotinamide, Anacardone (*B.D.H., London*), Coramine (*Ciba, Horsham*), Carrotone (*Boots, Nottingham*), Nicamide (*Burroughs Wellcome, London*).

CHARACTERS.

A colourless or yellowish oily liquid, or crystalline solid.

Miscible in all proportions with water, readily *soluble* in alcohol, in ether, in chloroform, and in acetone.

USES.

Powerful respiratory and cardiac stimulant.

DISPENSING.

Administered by mouth or injection. Solutions may be sterilized by autoclaving or by filtration.

DOSE.

3 to 8 gr. (0·2 to 0·5 gm.); by intravenous injection as a stimulant, 8 to 20 gr. (0·5 to 1·25 gm.).

NITROGENII MONOXIDUM (Nitrous Oxide).

CHARACTERS.

A colourless gas, with characteristic odour and sweet taste. *Soluble* in water (1 in 2 between 15° and 25°).

USES.

General anæsthetic.

NUX VOMICA (Nux Vomica).

The dried ripe seeds of *Strychnus Nux-vomica* Linn. Should contain not less than 1·25% strychnine.

CONSTITUENTS.

Strychnine and Brucine.

USES.

Bitter gastric stimulant. Tonic.

PREPARATIONS.

Nux Vomica Pulverata, B.P. (1·2% strychnine).—Powdered Nux Vomica. A standardized powder of nux vomica prepared by reducing it to a very fine powder, assaying and adjusting the strength, either by the addition of lactose or another sample of the drug, to 1·2% strychnine. *Dose*—1 to 4 gr. (0·06 to 0·25 gm.).

NOTE.—When Nux Vomica is prescribed this preparation must be dispensed.

Extractum Nucis Vomicæ Liquidum (1·5% w/v strychnine).—A brown liquid, obtained by percolating powdered nux vomica with alcohol (70%) to exhaustion, concentrating to low volume, and heating with hard paraffin, which is separated after cooling. It is then diluted with more alcohol (70%), and the percentage of strychnine in the solution is estimated, and enough alcohol (45%) added to make the resulting liquid extract contain 1½ gr. of the alkaloid—Strychnine—in 110 mins. *Dose*—1 to 3 min. (0·06 to 0·2 mil).

Extractum Nucis Vomicæ Siccum (5% strychnine).—A brown powder prepared by exhausting nux vomica by per-

colation with alcohol (70%), concentrating and defatting with hard paraffin as in the previous preparation. The liquid is then assayed, the calculated quantity of calcium phosphate added, and the whole evaporated to dryness, when it should contain 5% of strychnine. Industrial methylated spirit suitably diluted may replace the alcohol (70%) in this preparation. *Dose*—$\frac{1}{4}$ to 1 gr. (0·015 to 0·06 gm.).

Pilulæ Aloes et Nucis Vomicæ, B.P.C. (Pil. Aloes et Nuc. Vom.).—Aloes and Nux Vomica Pills. Each pill contains 2 gr. of aloes, $\frac{1}{4}$ gr. of dry extract of nux vomica and $\frac{1}{6}$ gr. of dry extract of belladonna. *Dose*—1 pill.

Tinctura Nucis Vomicæ, B.P. (Tinct. Nuc. Vom.).—Tincture of Nux Vomica. Liquid extract of nux vomica, 8·34% v/v, with alcohol (90%) and distilled water. It contains 0·125% w/v of strychnine; 30 min. contains about $\frac{1}{30}$ gr., and 2 mils contains about 0·0025 gm., of strychnine. *Dose*—10 to 30 min. (0·6 to 2 mils).

OLEUM AMYGDALÆ (Almond Oil).

CHARACTERS.

A pale yellow, bland and nutty fixed oil obtained by expression from the seeds of *Prunus communis* Arcang., var. *dulcis* Schneid., or *Prunus communis* Archang., var. *amara* Schneid. (sweet or bitter almonds).

DOSE.

$\frac{1}{2}$ to 1 fl. oz. (15 to 30 mils).

NOTE.—This harmless oil, which is commonly called almond oil, should not be confounded with the oil *distilled* from the bitter almond, which is known as the oil of bitter almonds, and which is a poison, being four times the strength of dilute hydrocyanic acid. It is not, however, in the Pharmacopœia. A purified oil of bitter almonds, free from hydrocyanic acid, is included in the 2nd Addendum to the B.P. 1932, and is described below.

OLEUM AMYGDALÆ VOLATILE PURIFICATUM (Purified Volatile Oil of Bitter Almonds).

A volatile oil prepared from the cake left after pressing the fixed oil from bitter almonds, peach kernels, or apricot kernels, by distillation with water. Hydrocyanic acid is removed from the distillate by treatment with ferrous sulphate and calcium hydroxide. This purified volatile oil contains not less than 95% of benzaldehyde.

CHARACTERS.

A colourless or pale yellow liquid ; odour and taste of bitter almonds.

USES.

Flavouring agent.

DOSE.

$\frac{1}{4}$ to 1 min. (0·016 to 0·6 mil).

OLEUM ARACHIS (Arachis Oil).

CHARACTERS.

The pale or greenish-yellow oil with nutty taste and odour expressed from the seeds of *Arachis hypogæa.*

USES.

In India and in the Eastern, African, and Australasian divisions of the Empire this oil may be employed in making the official liniments, ointments, plasters and soaps, instead of olive oil. See page 303 for war-time regulations.

PREPARATION

Emulsio Olei Arachis, B.P.C. (Emuls. Ol. Arach.).—Emulsion of Arachis Oil. *Syn.*—Marylebone Cream (Improved). Each fluid drachm contains about $\frac{1}{2}$ fl. dr. of arachis oil and solution of irradiated ergosterol equivalent to about 300 units of antirachitic activity. *Dose*—1 to 2 fl. dr. (4 to 8 mils).

OLEUM CADINUM (Oil of Cade).

SYNONYM.

Juniper Tar Oil.

CHARACTERS.

The brownish-black, oily, empyreumatic liquid obtained by the destructive distillation of the woody portions of *Juniperus oxycedrus* Linn.

USES.

Stimulating application in scaly skin diseases.

PREPARATION.

Ung. Olei Cadini, B.P.C. (Ung. Ol. Cadin.).—Ointment of Oil of Cade. Oil of cade, 25%, in yellow beeswax and yellow soft paraffin.

OLEUM CAJUPUTI (Oil of Cajuput).

CHARACTERS.

A colourless or yellow mobile oil, with camphoraceous odour, distilled from the leaves of *Melaleuca leucadendron* Linn. and other species.

USES.

Antispasmodic, antiseptic.

DOSE.

$\frac{1}{2}$ to 3 min. (0·06 to 0·2 mil).

PREPARATION.

Spiritus Cajuputi, B.P. (Sp. Cajuput.).—Spirit of Cajuput. Oil of cajuput, 10% v/v, in alcohol (90%). *Dose*—5 to 30 min. (0·3 to 2 mils).

OLEUM EUCALYPTI (Oil of Eucalyptus).

CHARACTERS.

A colourless liquid with a camphoraceous odour, obtained by distillation from fresh leaves of *Eucalyptis polybractea* R. T. Baker, and other species of eucalyptus.

USES.

Antiseptic, especially for the throat and chest.

DOSE.

1 to 3 min. (0·06 to 0·2 mil).

PREPARATIONS.

Nebula Eucalypti, B.P.C. (Neb. Eucalyp.).—Eucalyptus Spray. Oil of eucalyptus, 5% v/v, in light liquid paraffin.

Vapor Eucalypti Compositus, B.P.C. (Vap. Eucalyp. Co.). —Compound Eucalyptus Inhalation. *Syn.*—Anti-catarrhal Salts. Phenol, oil of eucalyptus, and camphor, of each about 1 in 6, oil of Siberian fir and strong solution of iodine, of each about 1 in 12, in ammoniated alcohol.

OLEUM HYDNOCARPI ÆTHYLICUM (Ethyl esters of Hydnocarpus Oil).

The ethyl esters of chaulmoogric and hydnocarpic acids. A colourless or yellow limpid oil.

USES.

Administered in leprosy.

DOSE.

5 to 15 min. (0·3 to 1 mil), increased gradually to 60 min. (4 mils), by the mouth; 30 min. (2 mils), increased gradually to 75 min. (5 mils), by subcutaneous and intramuscular injection.

OLEUM MENTHÆ PIPERITÆ (Oil of Peppermint).

CHARACTERS.

A pale yellow liquid with characteristic odour and taste, obtained by distillation from the fresh flower tops of *Mentha piperita* Linn.

USES.

Carminative.

DOSE.

1 to 3 min. (0·06 to 0·2 mil).

PREPARATION.

Spiritus Menthæ Piperitæ, B.P. (Sp. Menth. Pip.).—Spirit of Peppermint. *Syn.*—Essence of Peppermint. Oil of peppermint, 10% v/v, in alcohol (90%). *Dose*—5 to 30 min. (0·3 to 2 mils).

OLEUM IODISATUM (Iodised Oil).

SYNONYMS AND PROPRIETARY NAMES.

Oleum Iodatum, Iodatol (*British Drug Houses, London*), Iodinol (*Martindale, London*), Iodipin (*Merck, Darmstadt; Martindale, London*), Lipiodol (*Guerbert, Paris; Bengué, London*), Neo-Hydriol (*May & Baker, London*), Oliolase (*Corbière, Paris; Anglo-French Drug Co., London*).

CHARACTERS.

A colourless or pale yellow, viscous oil, being an iodine addition product of poppy seed oil.

USES.

For the diagnosis by X-ray of bronchiectasis.

STORAGE.

In well-filled containers protected from light.

OLEUM MORRHUÆ (Cod-liver Oil).

CHARACTERS.

A pale yellow oil obtained by expression from the fresh liver of the cod, *Gadus morrhua* Linn.

USES.

Antirachitic, and as a food.

DOSE.

$\frac{1}{4}$ to 2 fl. dr. (2 to 8 mils).

PREPARATIONS.

Emulsio Olei Morrhuæ, B.P. (Emuls. Ol. Morrh.).—Emulsion of Cod-liver Oil. It contains 50% v/v of cod-liver oil. *Dose*—$\frac{1}{4}$ to 1 fl. oz. (8 to 30 mils).

Emulsio Olei Morrhuæ cum Hypophosphitibus, B.P.C. (Emuls. Ol. Morrh. c. Hypophosph.).—Emulsion of Cod-liver Oil with Hypophosphites. *Syn.*—Emulsio Olei Morrhuæ Composita; Compound Emulsion of Cod-liver Oil. It contains 50% v/v of cod-liver oil with 1 gr. each of the hypophosphites of calcium and sodium in each fluid ounce. *Dose*—$\frac{1}{4}$ to 1 fl. oz. (8 to 30 mils).

Extractum Malti cum Olei Morrhuæ, B.P. (Ext. Malt. c. Ol. Morrh.).—Extract of Malt with Cod-liver Oil. Cod-liver oil, 10% w/w in extract of malt. It contains approximately 15% v/v of cod-liver oil; 4 fl. dr. contains about 30 min., and 16 mils contains about 2·5 mils of cod-liver oil. *Dose*—1 to 4 fl. dr. (4 to 16 mils).

OLEUM OLIVÆ (Olive Oil).

CHARACTERS.

A pale, yellow oil obtained by expression from the ripe fruits of *Olea europea* Linn.

USES.

Internally as a demulcent and food. Externally as an emollient.

DOSE.

$\frac{1}{2}$ to 1 fl. oz. (15 to 30 mils).

PREPARATIONS.

Emulsio Olei Olivæ, B.P.C. (Emuls. Ol. Oliv.).—Emulsion of Olive Oil. It contains 50% v/v of olive oil. *Dose*—$\frac{1}{4}$ to 1 fl. oz. (8 to 30 mils).

Linimentum Calcii Hydroxidi, B.P.C. (Lin. Calc. Hydrox.).—Liniment of Calcium Hydroxide. *Syn.*—Linimentum Calcis; Liniment of Lime. Solution of calcium hydroxide and olive oil, equal parts.

Unguentum Aquosum, B.P. (Ung. Aquos.).—Hydrous Ointment. Distilled water, about 25%, and borax, 1%, in white beeswax, white soft paraffin and olive oil.

OLEUM RICINI (Castor Oil).

CHARACTERS.

The viscid, almost odourless and colourless oil expressed from the seeds of *Ricinus communis* (Euphorbiaceæ). Taste at first bland and afterwards slightly acrid.

Soluble in alcohol (90%), 1 in $3\frac{1}{2}$.

USES.

A mild and speedy cathartic.

DOSE.

1 to 4 dr. (4 to 16 mils). For a child 1 year old, 1 dr.

OLEUM TEREBINTHÆ (Oil of Turpentine).

SYNONYM.

Rectified Oil of Turpentine.

CHARACTERS.

The limpid, colourless oil, distilled from the oleo-resin (crude turpentine) obtained from various species of Pinus, rectified by redistillation.

USES.

Antiseptic, carminative, rubefacient.

DOSE.

3 to 10 min (0·2 to 0·6 mil); as an anthelmintic, 2 to 4 dr. (8 to 16 mils) in an emulsion.

OLEUM THEOBROMATIS (Oil of Theobroma).

SYNONYMS.

Cacao Butter; Cocoa Butter.

CHARACTERS.

The yellowish, solid concrete oil, in cakes, expressed from the roasted seeds of *Theobroma Cacao*. (The seeds contain an alkaloid—Theobromine—which is a diuretic, acting like caffeine.)

USES.

Used in the preparation of all the suppositories except those with a glycerin basis.

OPIUM (Opium).

The partly-dried latex of *Papaver somniferum* Linn.

CONSTITUENTS.

Morphine, codeine, narcotine, thebaine and papaverine, with 13 other alkaloids.

USES.

Narcotic and anodyne.

PREPARATIONS.

Opium Pulveratum, B.P.—Powdered Opium. Prepared by reducing dried opium to a fine powder, assaying and adjusting with lactose so that it contains 10% morphine (anhydrous). A light brown powder with the odour and taste of opium. Used in the preparation of Pulv. Cret. Aromat. cum Opio, Pulv. Ipecac. et Opii, Suppos. Plumbi cum Opio. *Dose*—$\frac{1}{2}$ to 3 gr. (0·03 to 0·2 gm.).

NOTE.—When opium is prescribed, this preparation must be dispensed.

Extractum Opii Siccum, B.P. (Ext. Opii Sicc.).—Dry Extract of Opium. *Syn.*—Extractum opii aquosum I.A.; Extractum Opii. It is prepared with boiling water, and the macerate evaporated to dryness. It is adjusted with calcium phosphate to contain 20% of anhydrous morphine; 0·06 gm. contains 0·012 gm., and 1 gr. contains $\frac{1}{5}$ gr., of morphine. It should be stored in small, wide-mouthed, well-closed containers in a cool place. *Dose*—$\frac{1}{4}$ to 1 gr. (0·015 to 0·06 gm.).

Pulvis Cretæ Aromaticus cum Opio (2·5% opium).—A pale brown powder, composed of opium, cinnamon, nutmeg. clove, cardamom, sucrose. Carminative and anodyne, well adapted for children. *Dose*—10 to 60 gr. (0·6 to 4 gm.); for a child 1 year old, ½ to 1 gr.

Pulvis Ipecacuanhæ et Opii (10% opium).—*Syn.*—Dover's Powder; Pulv. Ipecac. Co. A fawn-coloured powder, composed of powdered ipecacuanha, powdered opium, and lactose. Diaphoretic. *Dose*—5 to 10 gr. (0·3 to 0·6 gm.).

Lotio Plumbi cum Opio, B.P.C. (Lot. Plumb. c. Opio).—Lead and Opium Lotion. Tincture of opium, 1 in 20, in dilute solution of lead subacetate.

Pilulæ Saponis cum Opio, B.P.C. (Pil. Sap. c. Opio).—Soap Pills with Opium. *Syn.*—Pilulæ Saponis Compositæ; Compound Soap Pills. Each pill contains ⅖ gr. of powdered opium and about 1 gr. of hard soap. *Dose*—1 or 2 pills.

Pulvis Kino Compositus, B.P.C. (Pulv. Kino Co.).—Compound Powder of Kino. Kino, 75%, and powdered opium, 5%, with cinnamon. *Dose*—5 to 20 gr. (0·3 to 1·2 gm.).

Suppositorium Plumbi cum Opio, B.P. (Supp. Plumb. c. Opio).—Suppository of Lead with Opium. *Syn.*—Suppositorium Plumbi Compositum. Each suppository contains 3 gr. (0·2 gm.) of lead acetate and 1 gr. (0·06 gm.) of powdered opium, equivalent to about $\frac{1}{10}$ gr. (0·006 gm.) of anhydrous morphine.

Tinctura Opii, B.P. (Tinct. Opii).—Tincture of Opium. *Syn.*—Laudanum. It is prepared by extracting opium with boiling water and alcohol. It contains 1% w/v of anhydrous morphine; 30 min. contains about ⅓ gr., and 2 mils contains 0·02 gm. of morphine. *Dose*—5 to 30 min. (0·3 to 2 mils).

Tinctura Opii Camphorata (0·05% morphine).—*Syn.*—Paregoric; Tinct. Camph. Co. A sherry-coloured liquid, composed of tincture of opium, benzoic acid, camphor, oil of anise, alcohol (60%). $\frac{1}{37}$ gr. morphine in 1 dr. *Dose*—½ to 1 dr. (2 to 4 mils); for a child 1 year old, 4 min. This is the only safe liquid preparation of opium for infants.

Unguentum Gallæ cum Opio, B.P.C. (Ung. Gall. c. Opio).—Gall and Opium Ointment. *Syn.*—Unguentum Gallæ Compositum. Powdered opium, 7·5%, in gall ointment.

ORTHOCAINA (Orthocaine).

SYNONYM AND PROPRIETARY NAME.

Orthoform (*Bayer Products, London*).

CHARACTERS.

A white or faintly yellow powder, odourless, tasteless. Slightly *soluble* in water, *soluble* 1 in 7 parts of alcohol.

USES.

Local anæsthetic, applied as a snuff, ointment or dusting powder.

DOSE.

$1\frac{1}{2}$ to 3 gr. (0·1 to 0·2 gm.).

PAMAQUINUM (Pamaquin).

SYNONYMS AND PROPRIETARY NAMES.

Plasmochin, Plasmoquine (*Bayer Products, London*), Praequine (*Pharmaceutical Specialists (May & Baker), London*).

CHARACTERS.

A yellow to orange yellow powder, taste bitter.

Insoluble in water; *soluble* 1 in 10 of water containing 5% acetone.

USES.

Antimalarial.

DOSE.

$\frac{1}{3}$ to $\frac{3}{5}$ gr. (0·02 to 0·04 gm.).

PANCREATINUM (Pancreatin).

A preparation obtained from the pancreas of certain animals which contains the enzymes trypsin, amylase and lipase.

CHARACTERS.

A colourless or buff-coloured powder with a meaty odour. *Soluble* in water, forming a turbid solution.

USES.

To aid digestion of protein and starch. Preferably administered in glutoid capsules (see p. 188).

DOSE.

3 to 10 gr. (0·2 to 0·6 gm.).

PREPARATIONS.

Liquor Pancreatini, B.P.C. (Liq. Pancreatin.).—Solution of Pancreatin. *Syn.*—Liquor Pancreatis; Pancreatic Solution. Glycerin of pancreatin, about 1 in 6, with sodium bicarbonate, glycerin, alcohol (90%) and distilled water. *Dose*—½ to 2 fl. dr. (2 to 8 mils).

Mistura Bismuthi et Pancreatini, B.P.C. (Mist. Bism. et Pancreatin.).—Mixture of Bismuth and Pancreatin. Each fluid ounce contains 10 gr. each of bismuth carbonate and sodium bicarbonate, 4 gr. of pancreatin, and 4 min. of dilute hydrocyanic acid, in chloroform water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

PARAFFINUM DURUM (Hard Paraffin).

CHARACTERS.

A colourless, translucent, waxy-looking substance, melting between 50° and 60°, being a mixture of several of the harder members of the paraffin series of hydrocarbons, and obtained from petroleum and from shale oil.

USES.

A basis for ointments.

PARAFFINUM LIQUIDUM (Liquid Paraffin).

CHARACTERS.

A clear, colourless, odourless, non-fluorescent, oily liquid, being a mixture of liquid hydrocarbons obtained from petroleum.

USES.

Lubricant and sedative for mucous surfaces.

DOSE.

¼ to 1 fl. oz. (7·5 to 30 mils).

NOTE.—The official quality is suitable for internal administration, but when required for nasal sprays a liquid paraffin of lower viscosity is preferable (Paraff. Liquid. Leve.).

PREPARATIONS.

Emulsio Paraffini Liquidi Composita, B.P.C. (Emuls. Paraff. Liq. Co.).—Compound Emulsion of Liquid Paraffin. *Syn.*—Emulsion of Liquid Paraffin with Agar and Phenolphthalein. Emulsion of liquid paraffin with agar containing

$1\frac{1}{2}$ gr. of phenolphthalein in each fluid ounce. *Dose*—1 to 4 fl. dr. (4 to 10 mils).

Emulsio Paraffini Liquidi cum Agar, B.P.C. (Emuls. Paraff. Liq. c. Agar).—Emulsion of Liquid Paraffin with Agar. It contains 50% v/v of liquid paraffin, with agar. *Dose*—1 to 4 fl. dr. (4 to 16 mils).

Emulsio Paraffini Liquidi et Kaolini, B.P.C. (Emuls. Paraff. Liq. et Kaolin.).—Emulsion of Liquid Paraffin and Kaolin. It contains liquid paraffin, 23% v/v, and kaolin, 18·75% w/v ; each fluid ounce contains 2 fl. dr. of liquid paraffin and about 80 gr. of kaolin. *Dose*—$\frac{1}{2}$ to 2 fl. dr. (16 to 60 mils).

Mistura Magnesii Hydroxidi et Paraffini Liquidi, B.P.C. (Mist. Magnes. Hydros. et Paraff. Liq.).—Mixture of Magnesium Hydroxide and Liquid Paraffin. Liquid paraffin, 30% v/v, with mixture of magnesium hydroxide, flavoured with vanillin. *Dose*—1 to 4 fl. dr. (4 to 16 mils).

PARAFFINUM LIQUIDUM LEVE (Light Liquid Paraffin).

CHARACTERS.

A clear, colourless, oily liquid, free from fluorescence by daylight, being a mixture of liquid hydrocarbons obtained from petroleum. About half the kinematic viscosity of Liquid Paraffin.

USES.

As for Liquid Paraffin, but more suitable for atomizing from a spray solution.

PARAFFINUM MOLLE (Soft Paraffin).

SYNONYMS AND PROPRIETARY NAMES.

Petrolatum, Petroleum Jelly, Vaselina, Vaselinum, Vaseline (*Chesebrough Manufacturing Co., London*).

CHARACTERS.

A translucent, semisolid, unctuous substance, being a mixture of the soft members of the paraffin series of hydrocarbons ; usually obtained by purifying the less volatile portions of petroleum. It is commonly known as Vaseline, and exists in the *white* and *yellow* varieties. Emollient and protective. Enters into 11 official ointments.

PREPARATIONS.

Unguentum Paraffini.—Paraffin Ointment. A yellow or white ointment, obtained by melting together hard paraffin and soft paraffin (white or yellow) and white beeswax. Used as a basis for Ung. Acid. Boric., and Ung. Acid. Salicyl.

Unguentum Simplex.—Simple Ointment. A yellow or white ointment, obtained by melting together wool fat, hard paraffin and yellow or white soft paraffin. This is a softer basis than Ung. Paraffin., and is used for the following ointments: Ung. Chrysarob., Ung. Hyd. Ammon., Ung. Hyd. Oleat., Ung. Hyd. Subchlor., Ung. Sulph., Ung. Zinci Oxid.

PARALDEHYDUM (Paraldehyde).

CHARACTERS.

A colourless liquid with a strong odour and burning taste. *Soluble* 1 in 9 parts of water. *Miscible* with alcohol.

USES.

Hypnotic.

DISPENSING.

Either administered as a solution in water, or if the amount is in excess of solubility suspended with mucilage of tragacanth. The taste is often disguised with liquid extract of liquorice. Also given as an enema.

DOSE.

½ to 2 dr. (2 to 8 mils).

PELLETIERINÆ TANNAS (Pelletierine tannate).

CHARACTERS.

A light yellow amorphous powder with an astringent taste, being a mixture of the tannates of the alkaloids obtained from the bark of the root and stem of *Punica Granatum*.

Soluble 1 in about 700 of water.

USES.

Anthelmintic for the tape worm.

DOSE.

2 to 8 gr. (0·12 to 0·5 gm.).

PEPSINUM (Pepsin).

CHARACTERS.

Colourless or yellowish white amorphous powder, or in thin translucent scales.

Soluble in water, forming an opalescent solution.

USES.

To increase the digestive power of the gastric secretions.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

PREPARATIONS.

Glycerinum Pepsini, B.P.C. (Glycer. Pepsin.).—Glycerin of Pepsin. Pepsin, 10% w/v, with hydrochloric acid, glycerin and distilled water. *Dose*—1 to 2 fl. dr. (4 to 8 mils).

Mistura Bismuthi Composita cum Pepsino, B.P.C. (Mist. Bism. Co. c. Pepsin.).—Compound Bismuth Mixture with Pepsin. Each fluid drachm contains ½ fl. dr. of concentrated solution of bismuth, 1 gr. of pepsin, 7½ min. of tincture of nux vomica and 2 min. of dilute hydrocyanic acid, with chloroform, solution of bordeaux B and distilled water. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

PHEMITONUM (Phemitone).

PROPRIETARY NAME.

Prominal (*Bayer Products, London*).

CHARACTERS.

White crystalline powder, odourless, tasteless. Almost *insoluble* in water; *soluble* in alcohol, ether, chloroform, and alkali hydroxides.

USES.

Anti-epileptic, antispasmodic and hypnotic.

DOSE.

½ to 6 gr. (0·03 to 0·4 gm.).

PHENACETINUM (Phenacetin).

CHARACTERS.

Colourless, tasteless, inodourous, scaly crystals.

Soluble 1 in about 1700 parts of water.

USES.

Antipyretic and analgesic.

DISPENSING.

Administered in tablets or cachets or in mixtures suspended with Compound Power of Tragacanth. Frequently dispensed with caffeine and/or aspirin.

DOSE.

5 to 10 gr.

PREPARATIONS.

Tabellæ Acidi Acetylsalicylici Compositæ, B.P.C. (Tab. Acid. Acetylsalicyl. Co.).—Compound Tablets of Acetylsalicylic Acid. *Syn.*—Compound Aspirin Tablets. Each tablet contains 3½ gr. of acetyl-salicylic acid, 2½ gr. of phenacetin and ½ gr. of caffeine. *Dose*—1 or 2 tablets.

Haustus Acidi Acetylsalicylici Compositus (Middlesex Hospital).—Acetylsalicylic acid, 5 gr., phenacetin, 5 gr., caffeine, 2 gr., compound powder of tragacanth, 10 gr., chloroform water, to 1 oz. *Dose*—1 fl. oz.

PHENAZONUM (Phenazone).

CHARACTERS.

Colourless, inodorous, bitter, scaly crystals.
Soluble 1 in 12 of water.

USES.

Antipyretic and analgesic.

DISPENSING.

Incompatible with Spiritus Ætheris Nitrosi and other nitrites.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

PHENOBARBITONUM (Phenobarbitone).

SYNONYMS AND PROPRIETARY NAMES.

Phenylethylmalonylurea, Luminal (*Bayer Products, London*); Gardenal (*May & Baker, London*).

CHARACTERS.

A white crystalline powder, odourless, slightly bitter taste. *Soluble* 1 in about 1000 parts of water.

USES.

Hypnotic and sedative.

DOSE.

½ to 2 gr. (0·03 to 0·12 gm.).

PREPARATIONS.

Phenobarbitonum Solubile (Soluble Phenobarbitone). *Syn. and proprietary names.*—Phenobarbitone-Sodium, Gardenal-Sodium (*May & Baker, London*); Luminal Sodium (*Bayer Products, London*). A white hygroscopic powder *soluble* in water. Hypnotic and sedative. *Dose*—½ to 2 gr. (0·03 to 0·12 gm.).

PHENOL (Phenol).

SYNONYM.

Carbolic acid.

CHARACTERS.

Colourless, deliquescent, needle-shaped crystals, or crystalline masses, characteristic odour and sweet taste.

Soluble 1 in 13 parts of water, 3 in 1 part of glycerin, 1 in about 200 parts of liquid paraffin.

USES.

Antiseptic.

DOSE.

1 to 3 gr. (0·06 to 0·2 gm.).

PREPARATIONS.

Phenol Liquefactum, B.P. (Phenol. Liq.).—Liquefied Phenol. *Syn.*—Acidum Carbolicum Liquefactum. Phenol, 80% w/w, with water. Specific gravity, about 1·063. Boiling-point, gradually rising to a temperature not higher than 183°. When phenol is to be mixed with collodion, fixed oils, or paraffin, melted phenol should be used, not liquefied phenol. It should be stored in well-closed containers and protected from light. *Dose*—1 to 3 min. (0·06 to 0·2 mil).

Glycerinum Phenolis, B.P. (Glycer. Phenol.).—Glycerin of Phenol. *Syn.*—Glycerinum Acidi Carbolici. Phenol, 16%.

w/w, dissolved in glycerin. *Caution.*—Dilution with water renders it caustic; it may be diluted with glycerin. *Dose*—5 to 15 min. (0·3 to 1 mil).

Lotio Phenolis, B.P.C. (Lot. Phenol.).—Phenol Lotion. *Syn.*—Lotio Acidi Carbolici; Carbolic Acid Lotion. Phenol, 1 in 80, in distilled water, coloured with solution of bordeaux B.

Solutio phenoli I.A. contains 2% of phenol.

Trochiscus Phenolis, B.P. (Troch. Phenol.).—Lozenge of Phenol. *Syn.*—Trochiscus Acidi Carbolici; Phenol Lozenge; Carbolic Acid Lozenge. Each lozenge contains approximately $\frac{1}{2}$ gr. (0·03 gm.) of phenol in a basis coloured with carmine. These lozenges should be stored in well-closed containers in a cool place and protected from light.

Unguentum Phenolis, B.P. (Ung. Phenol.).—Ointment of Phenol. *Syn.*—Unguentum Acidi Carbolici; Phenol Ointment. Phenol, 3%, in a mixture of white beeswax, lard and hard and soft paraffins.

PHENOLPHTHALEINUM (Phenolphthaleinum).

PROPRIETARY NAME.

Laxoin (*Oppenheimer*, *London*).

CHARACTERS.

A white, tasteless, crystalline or amorphous powder.

Almost *insoluble* in water, *soluble* 1 in 10 parts of alcohol (90%).

USES.

Purgative.

DOSE.

1 to 5 gr. (0·06 to 0·3 gm.).

PREPARATIONS.

Emulsio Paraffini Liquidi Composita, B.P.C. (Emuls. Paraff. Liq. Co.).—Compound Emulsion of Liquid Paraffin. *Syn.*—Emulsion of Liquid Paraffin with Agar and Phenolphthalein. Emulsion of liquid paraffin with agar, containing $1\frac{1}{2}$ gr. of phenolphthalein in each fl. oz. *Dose*—1 to 4 fl. dr. (4 to 16 mils).

Tabellæ Phenolphthaleini Compositæ, B.P.C. (Tab. Phenolphthal. Co.).—Compound Phenolphthalein Tablets. Each tablet contains 1 gr. of phenolphthalein, $\frac{1}{100}$ gr. of dry extract of belladonna, and $\frac{1}{500}$ gr. of strychnine sulphate. *Dose*—1 to 3 tablets.

PHENYLHYDRARGYRI NITRAS (Phenylmercuric Nitrate).

PROPRIETARY NAME.

Merfenil (*May & Baker, London*).

CHARACTERS.

A white substance, sparingly *soluble* in water, 1 in 160 of boiling water.

USES.

As a bactericide in the form of lotion, for skin affections (1 in 3000), wounds (1 in 1500), or used as a vaginal douche (1 in 30,000). An 0·002% concentration is used in sterilizing solutions by steaming.

PHYSOSTIGMINÆ SALICYLAS (Physostigmine Salicylate).

SYNONYM.

Eserine Salicylate.

CHARACTERS.

Colourless or faintly yellow, odourless crystals.

Soluble 1 in about 100 parts of water, and 1 in about 12 of alcohol (90%).

USES.

Myotic. Used internally as hypodermic injection to open the bowels in acute abdominal conditions.

DISPENSING.

Solutions for injection may be sterilized by heating with a bactericide or filtration. Glass containers should comply with the limit test for alkalinity of glass. Solutions rapidly become pink in colour. This colour change is hastened if solutions are made alkaline. Prepare solution with freshly boiled and cooled distilled water.

DOSE.

$\frac{1}{100}$ to $\frac{1}{50}$ gr. (0·0006 to 0·0012 gm.).

PREPARATIONS.

Guttæ Physostigminæ, B.P.C. (Gutt. Physostig.).—Physo-

stigmine Eye Drops. *Syn.*—Guttæ Eserinæ; Eserine Eye Drops. Physostigmine salicylate, 1%, with boric acid, in sterilized water.

Oculentum Physostigminæ, B.P. (Oculent. Physostig.).—Physostigmine Ointment for the Eye. *Syn.*—Oculentum Eserinæ. Physostigmine salicylate, 0·125%, in simple eye ointment. It should be stored in small, well-closed containers in a cool place and protected from light.

PILOCARPINÆ NITRAS (Pilocarpine Nitrate).

CHARACTERS.

Minute circular crystals, or crystalline powder, without odour but with a faintly bitter taste.

Soluble 1 in 8 parts of water and 1 in 50 parts of alcohol (90%).

USES.

Powerful sudorific and sialogogue.

DISPENSING.

Solutions for injection may be sterilized by autoclaving or by filtration. Glass containers should comply with the limit test for alkalinity in glass.

DOSE.

$\frac{1}{20}$ to $\frac{1}{5}$ gr. (0·003 to 0·12 gm.).

PITUITARII, EXTRACTUM LIQUIDUM (Pituitary (Posterior Lobe) Extract).

SYNONYMS AND PROPRIETARY NAMES.

Glanduitrin (*Richter*, *London*); Hypophysin (*Bayer Products*, *London*); Infundibulin (*Evans*, *Sons*, *Lescher & Webb*, *Liverpool*); Infundin (*Burroughs Wellcome*, *London*); Liquor Pituitarii, Pitibulin (*Allen & Hanburys*, *London*); Pitoxylin (*Oxo*, *London*); Pituitrin (*Parke Davis*, *London*); Solution of Pituitary.

CHARACTERS.

An aqueous extract of the posterior lobes of pituitary bodies of oxen or other mammals, containing 10 units per mil. The pituitary bodies, on removal from the animals, are imme-

diately frozen. When used they are trimmed, minced, and extracted with a hot very dilute solution of acetic acid (*p*H 3 to *p*H 4). The solution is filtered, assayed, diluted to the correct strength, and the acidity readjusted. It is then placed in sterile glass containers sealed. Sterilization is effected either by previous filtration or by autoclaving after sealing. If several doses are included in one container, an antiseptic should be added.

STORAGE.

Should be kept at as low a temperature as possible above its freezing-point. Under these conditions the product may be expected to retain its potency for at least eighteen months after the date of manufacture, provided that the reaction lies between the limits *p*H 3 and *p*H 4.

LABELLING.

The label on each container states the number of units per mil.

USES.

To stimulate uterine contractions during labour, and to control post partum hæmorrhage.

DOSE.

By subcutaneous injection, 2 to 5 units (0·2 to 0·5 mil.)

NOTE.—The preparation only remains active if the *p*H lies between 3 and 4. Alkali quickly inactivates it. All glass containers must be free from alkali.

OTHER PITUITARY PREPARATIONS.

Pitocin (*Parke Davis, London*) and Uteritin (*Richter, London*) are solutions of the oxytocic principle. Pitressin (*Parke Davis, London*). is a solution of the pressor principle.

Pituitary (Anterior Lobe) Extract. *Proprietary Names.*—Antoxylin (*Oxo, London*), Antuitrin (*Parke Davis, London*), Pitexan (capsules for oral use) (*Paines & Byrne, London*), Præphyson (*Promonta, Hamburg*; *Pharmaceutical Products, London*).

PIX CARBONIS PRÆPARATA (Prepared Coal Tar).

CHARACTERS.

Obtained by placing commercial coal tar in a shallow vessel, and maintaining it at a temperature of 50° for one hour, stirring

frequently. A black viscous liquid with a strong empyreumatic odour.

USES.

Antiseptic. Applied externally for skin diseases as lotion, paste or ointment.

PREPARATIONS.

Liquor Picis Carbonis, B.P. (Liq. Pic. Carbon.).—Solution of Coal Tar. It is prepared by macerating prepared coal tar, 20% w/v, and quillaia in alcohol (90%) or in industrial methylated spirit, suitably diluted.

Pasta Picis Carbonis, B.P.C. (Past. Pic. Carbon.).—Coal Tar Paste. Coal tar, about 3·5%, with compound paste of zinc oxide.

Unguentum Picis Carbonis, B.P.C. (Ung. Pic. Carbon.).—Coal Tar Ointment. Solution of coal tar, about 0·25 % in yellow soft paraffin.

PIX LIQUIDA (Tar).

SYNONYM.

Stockholm tar.

CHARACTERS.

A blackish, viscous substance with strong characteristic odour, obtained by destructive distillation of *Pinus sylvestris* Linn., and other members of the family *Pinaceæ*.

USES.

Antiseptic and expectorant.

DOSE.

2 to 10 gr. (0·12 to 0·6 gm.).

PREPARATIONS.

Syrupus Pini Albi Compositus, B.P.C. (Syr. Pini Alb. Co.)—Compound Syrup of White Pine. Liquid extract of white pine, 1 in 20, and syrup of tar, 1 in 5, with liquid extract of squill, solution of bordeaux B, ammonium chloride, sucrose, glycerin and distilled water. *Dose*—*1 to 2 fl. dr. (4 to 8 mils).*

Unguentum Picis Liquidæ, B.P.C. (Ung. Pic. Liq.).—Tar. Ointment. Tar, 70%, in lard and yellow beeswax.

Unguentum Sulphuris Compositum, B.P.C. (Ung. Sul-

phur. Co.).—Compound Sulphur Ointment. Sublimed sulphur and tar, of each, 15%, and calcium carbonate, 10%, in lard and soft soap.

PLUMBI ACETAS (Lead Acetate).

SYNONYM.

Sugar of Lead.

CHARACTERS.

White, crystalline, slightly efflorescent masses.

Soluble 1 in 2·5 parts of water, 1 in 2 of glycerin, and 1 in 30 of alcohol (90%).

USES.

Astringent. Internally, to arrest diarrhœa; externally, as a lotion for the skin or vagina. Suppositories, often with opium, are used for piles.

DISPENSING.

Solutions should be prepared with recently boiled and cooled distilled water. Incompatible with carbonates, chlorides, iodides, sulphates, phosphates and tannic acid.

DOSE.

½ to 2 gr. (0·03 to 0·12 gm.).

PREPARATIONS.

Glycerinum Plumbi Subacetatis, B.P.C. (Glycer. Plumb. Subacet.)—Glycerin of Lead Subacetate. A glycerin solution of the residue obtained by evaporating strong solution of lead subacetate.

Liquor Plumbi Subacetatis Dilutus, B.P. (Liq. Plumb. Subacet. Dil.).—Dilute solution of Lead Subacetate. *Syn.*—Liquor Plumbi Subacetatis; Goulard's Lotion; Goulard's Water; Lotio Plumbi; Lead Lotion; Liquor Plumbi. Strong solution of lead subacetate, 1 in 80, in distilled water. It should be freshly prepared.

Liquor Plumbi Subacetatis Fortis, B.P. (Liq. Plumb. Subacet. Fort.).—Strong Solution of Lead Subacetate. *Syn.*—Goulard's Extract; Liquor Plumbi Fortis. It contains not less than 19% and not more than 21·5% w/w of total Pb, and has an alkalinity corresponding to not less than 10·2%, and not more than 11·6% w/w of PbO. It should be stored in well-filled, well-closed containers.

Lotio Plumbi cum Opio, B.P.C. (Lot. Plumb. c. Opio).—Lead and Opium Lotion. Tincture of opium, 1 in 20, in dilute solution of lead subacetate.

Lotio Plumbi Evaporans, B.P.C. (Lot. Plumb. Evap.).—Evaporating Lead Lotion. Strong solution of lead subacetate, 1 in 80, and alcohol (90%), 1 in 5, in distilled water.

Suppositorium Plumbi cum Opio, B.P. (Supp. Plumb. c. Opio).—Suppository of Lead with Opium. *Syn.*—Suppositorium Plumbi Compositum. Each suppository contains 3 gr. (0·2 gm.) of lead acetate and 1 gr. (0·06 gm.) of powdered opium, equivalent to about $\frac{1}{10}$ gr. (0·006 gm.) of anhydrous morphine.

Emplastrum Plumbi, B.P.—Lead Plaster. *Syn.*—Diachylon; Diachylon Plaster. A pale yellow solid, consisting of oleate, palmitate, and stearate of lead, and a little glycerin; it is, chemically speaking, a *soap*. It is prepared by boiling in a steam-bath lead oxide, olive oil, and water, *q.s.*, till a proper consistence is obtained. Used for preparing Emp. Colophonii.

PODOPHYLLUM (Podophyllum).

The dried rhizome and roots of *Podophyllum peltatum* Linn.

USES.

Cholagogue and aperient.

DOSE.

2 to 10 gr. (0·13 to 0·6 gm.).

PREPARATIONS.

Podophylli Resina.—Podophyllum Resin. *Syn.*—Podophyllin. A pale greenish-brown powder, prepared by pouring a concentrated alcoholic tincture of podophyllum or Indian podophyllum into water acidulated with hydrochloric acid, when the resin is precipitated; it is afterwards washed and dried. *Dose*—$\frac{1}{4}$ to 1 gr. (0·015 to 0·06 gm.).

Pilulæ Aloini et Podophyllini Compositæ, B.P.C. (Pil. Aloin. et Podoph. Co.).—Compound Aloin and Podophyllin Pills. Each pill contains $\frac{1}{10}$ gr. each of aloin and jalap resin, $\frac{1}{100}$ gr. of oleoresin of capsicum, $\frac{1}{20}$ gr. each of the dry extracts of nux vomica and hyoscyamus, and about $\frac{1}{6}$ gr. of resin of podophyllum. *Dose*—1 to 4 pills.

Pilulæ Podophyllini, Belladonnæ et Nucis Vomicæ, B.P.C. (Pil. Podoph. Bellad. et Nuc. Vom.).—Podophyllin,

Belladonna and Nux Vomica Pills. Each pill contains $\frac{1}{3}$ gr. each of resin of podophyllum, dry extract of belladonna and dry extract of nux vomica, and 1 gr. of aloes. *Dose*—1 or 2 pills.

Pilulæ Podophyllini Compositæ, B.P.C. (Pil. Podoph. Co.).—Compound Podophyllin Pills. Each pill contains $\frac{1}{4}$ gr. of resin of podophyllum, 1 gr. of mercurous chloride and $\frac{1}{8}$ gr. of dry extract of belladonna. *Dose*—1 pill.

Tinctura Podophylli, B.P.C. (Tinct. Podoph.).—Tincture of Podophyllum. Resin of podophyllum, about 1 in 30. *Dose*—5 to 15 min. (0·3 to 1 mil).

POTASSA SULPHURATA (Sulphurated Potash).

SYNONYM.

Liver of Sulphur.

CHARACTERS.

Solid greenish-yellow fragments, yellowish brown within. *Soluble* 1 in 2 parts of water.

STORAGE.

Well-losed containers.

USES.

Used externally as a lotion, bath, or ointment for skin affections.

PREPARATIONS.

Lotio Potassæ Sulphuratæ, B.P.C. (Lot. Potass. Sulphurat.).—Lotion of Sulphurated Potash. *Syn.*—Lotio Zinci Sulphidi. Each fluid ounce contains zinc sulphide, prepared from 10 gr. of sulphurated potash and 10 gr. of zinc sulphate, in rose water.

Sal Aperiens Sulphuratum, B.P.C. (Sal Aper. Sulphurat.).—Sulphurated Aperient Salt. *Syn.*—Harrogate Salts. Sulphurated potash, 3%, and potassium acid tartrate, 15%, with exsiccated magnesium sulphate. *Dose*—1 to 2 dr. (4 to 8 gm.).

Unguentum Potassii Polysulphidi, B.P.C. (Ung. Potass. Polysulph.).—Potassium Polysulphide Ointment. *Syn.*—Marcussen's Ointment; Danish Ointment. It contains polysulphides of potassium equivalent to 12·5% of sublimed sulphur, with zinc hydroxide and benzaldehyde, in wool fat, yellow soft paraffin and liquid paraffin.

POTASSII ACETAS (Potassium Acetate).

CHARACTERS.

White deliquescent, satiny, masses or granular particles. *Soluble* 2 in 1 part of water, and 1 in 2 parts of alcohol.

USES.

Diuretic.

DISPENSING.

Often given with Infusion of Buchu.

DOSE.

15 to 60 gr. (1 to 4 gm.). 3 gr. for a child 1 year old.

PREPARATION.

Mistura Potassii Acetatis Composita, B.P.C. (Mist. Pot. Acet. Co.).—Compound Potassium Acetate Mixture. *Syn.*—Mistura Diuretica. Each fluid ounce contains 20 gr. of potassium acetate, 30 min. of spirit of nitrous ether, 20 min. of tincture of hyoscyamus and 60 min. of juice of soparium, with infusion of buchu. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

POTASSII BICARBONATIS (Potassium Bicarbonate).

CHARACTERS.

Colourless prismatic crystals, or white granular powder. *Soluble* 1 in 4 parts of water.

USES.

Antacid.

DISPENSING.

Often given as an effervescent draught with citric acid or lemon juice. 20 gr. are neutralized by 14 gr. of citric or 15 gr. of tartaric acid.

DOSE.

15 to 60 gr. (1 to 4 gm.).

POTASSII BROMIDUM (Potassium Bromide).

CHARACTERS.

Colourless crystals, or white granular powder, with a strong saline taste.

Soluble 1 in 2 parts of water.

USES.

Hypnotic, sedative.

DISPENSING.

Usually administered in solution or tablets. Tablets should be dissolved in water before swallowing. Liquid Extract of Liquorice is useful in disguising the saline taste.

DOSE.

5 to 30 gr. (0·3 to 2·0 gm.) in solution.

PREPARATIONS.

Liquor Bromidi Compositus, B.P.C. (Liq. Brom. Co.).—Compound Bromide Solution. *Syn.*—Liquor Bromochloral Compositus. Each fluid drachm contains 15 gr. of chloral hydrate and 15 gr. of potassium bromide, with extract of cannabis, liquid extract of hyoscyamus, tincture of orange, glycerin and distilled water. *Dose*—½ to 2 fl. dr. (2 to 8 mils).

Mistura Bromidi Composita, B.P.C. (Mist. Brom. Co.).—Compound Mixture of Bromides. Each fluid ounce contains 10 gr. each of the bromides of ammonium, potassium and sodium, with tincture of nux vomica and solution of carmine, glycerin and chloroform water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

POTASSII CHLORAS (Potassium Chlorate).

CHARACTERS.

Colourless crystals, or a white powder.
Soluble 1 in 16 parts of water.

USES.

As a mouthwash, pastille, lozenge, or gargle in inflamed conditions of the mouth or throat.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

PREPARATIONS.

Gargarisma Chlori, B.P.C. (Garg. Chlor.).—Chlorine Gargle. A chlorinated solution prepared by dissolving in water the products of the interaction of potassium chlorate and hydrochloric acid. It should be diluted before use with one or more parts of water.

Gargarisma Potassii Chloratis, B.P.C. (Garg. Pot.

Chlorat.). –Potassium Chlorate Gargle. Potassium chlorate, about 1 in 40, in distilled water acidified with dilute hydrochloric acid.

Trochisci Potassii Chloratis, B.P.C. (Troch. Pot. Chlorat.). —Potassium Chlorate Lozenges. Each lozenge contains 3 gr. of potassium chlorate.

POTASSII CITRAS (Potassium Citrate).

CHARACTERS.

White granular crystals, or crystalline powder, with a saline taste.

Soluble 1 in 1 part of water.

USES.

Diuretic, diaphoretic. Renders the urine alkaline.

DOSE.

15 to 60 gr. (1 to 4 gm.), in water.

PREPARATIONS.

Mistura Ammonii Acetatis Composita, B.P.C. (Mist. Ammon. Acet. Co.).—Compound Ammonium Acetate Mixture. *Syn.*—Mistura Diaphoretica. Each fluid ounce contains 20 gr. of potassium citrate and 20 min. each of strong solution of ammonium acetate, spirit of nitrous ether and spirit of chloroform, in camphor water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Potassii Citras Effervescens, B.P.C. (Pot. Cit. Efferv.).—Effervescent Potassium Citrate. About 1 in 6. *Dose*—1 to 2 dr. (4 to 8 gm.).

POTASSII IODIDUM (Potassium Iodide).

CHARACTERS.

Colourless, odourless, cubical crystals, or white granular powder.

Soluble 1 in 0·7 parts of water.

USES.

Used in the treatment of syphilis, goitre, and externally as a liniment for enlarged glands.

DISPENSING.

Incompatible with spirit of nitrous ether, dilute nitro-hydrochloric acid, potassium chlorate and solutions of ferric chloride. All these substances liberate iodine.

DOSE.

5 to 30 gr. (0·3 to 2·0 gm.).

PREPARATION.

Linimentum Potassii Iodidi cum Sapone, B.P.C. (Lin. Pot. Iod. c. Sap.).—Liniment of Potassium Iodide with Soap. A solid preparation containing potassium iodide, about 1 in 7, with curd soap, glycerin, oil of lemon and distilled water.

POTASSII PERMANGANAS (Potassium Permanganate).

CHARACTERS.

Dark purple, iridescent, slender, prismatic crystals, with an astringent taste.

Soluble, 1 in 20 parts of water.

USES.

Deodorant, antiseptic; used as lotion, gargle, mouthwash, or vaginal injection.

DISPENSING.

If administered in pill form, the mass should be made with wool fat and stiffened with kaolin.

DOSE.

1 to 3 gr. (0·06 to 0·2 gm.).

PREPARATION.

Liquor Potassii Permanganatis, B.P.C. (Liq. Pot. Permang.).—Solution of Potassium Permanganate. 1% w/v. *Dose*—2 to 4 fl. dr. (8 to 15 mils).

POTASSII TARTRAS ACIDUS (Potassium Acid Tartrate).

SYNONYM.

Purified Cream of Tartar.

CHARACTERS.

A white, gritty, crystalline powder.

Soluble 1 in 220 parts of water.

USES.

Purgative.

DISPENSING.

Commonly dispensed as **Pulvis** Jalapæ Compositus or Confectio Sulphuris.

DOSE.

15 to 60 gr.

PREPARATION.

Potus Imperialis, B.P.C. (Potus Imperial.).—Imperial Drink. *Syn.*—Haustus Imperialis. Potassium acid tartrate, 0·45% w/v, with citric acid, sucrose, oil of lemon and tincture of lemon, in distilled water; each fluid ounce contains 2 gr. of potassium acid tartrate.

PROCAINÆ HYDROCHLORIDUM (Procaine Hydrochloride).

SYNONYMS AND PROPRIETARY NAMES.

Ethocaine Hydrochloride, *p*-Aminobenzýldiethylaminœthanol, Allocaine, Syncainæ, Æthocaine (*Nederlandsche Cocainefabriek, Amsterdam; Greef, London*), Kerocain (*Kerfoot, Barnsley*), Neocaine (*Corbière, Paris; Anglo-French Drug Co., London*), Növocaine (*Bayer-Meister Lucius, Leverkusen; Saccharin Corporation, London*), Planocaine (*May & Baker, London*).

CHARACTERS.

A colourless crystalline powder, odourless, slightly bitter taste, followed by a temporary insensibility of the tongue.

Soluble 1 in 1 part of water, 1 in 8 parts of alcohol (90%).

USES.

Local anæsthetic.

DISPENSING.

Solutions for injection may be sterilized by filtration or tyndallization. Glass containers should comply with the limit test for alkalinity of glass.

DOSE.

½ to 2 gr. (0·03 to 0·12 gm.); up to 15 gr. by subcutaneous injection; up to 2½ gr. (0·15 gm.) by intrathecal injection.

PROFLAVINÆ SULPHAS (Proflavine Sulphate).

CHARACTERS.

Orange red to brownish red, crystalline powder ; odourless. *Soluble*, 1 in 300 of water, 1 in 10 of glycerin, almost *insoluble* in ether and liquid paraffin.

USES.

As a bactericide. It is stated to be less toxic to brain tissue than acriflavine.

DISPENSING.

Unlike acriflavine, it is compatible with sodium chloride solution. A 1 in 1000 or 1 in 2000 solution is often used.

PRUNUS SEROTINA (Wild Cherry Bark).

The bark of the wild or black cherry *Prunus serotina* Ehrhardt.

USES.

Much used to relieve cough.

DOSE.

15 to 30 gr. (1 to 2 gm.).

PREPARATION.

Syrupus Pruni Serotinæ, B.P. (Syr. Prun. Serot.).—Syrup of Wild Cherry. *Syn.*—Syrupus Pruni Virginianæ ; Syrup of Virginian Prune. A solution of sucrose in the liquid obtained by percolating wild cherry bark with glycerin and water ; it contains active constituents equivalent to 15% w/v of the bark. It should be stored in well-closed containers in a cool place. *Dose*—½ to 2 fl. dr. (2 to 8 mils).

PULVIS VITAMINI B_1 (Adsorbate of Vitamin B_1).

CHARACTERS.

An adsorbate of the antineuritic vitamin (vitamin B_1) on fuller's earth. One gramme contains 100 units of antineuritic activity.

USES.

Therapeutic and prophylactic use in beriberi.

DOSE.

Prophylactic (daily), 15 to 30 gr. (1 to 2 gm.); 100 to 200 units. Therapeutic (daily), 30 to 90 gr. (2 to 6 gm.); 200 to 600 units.

QUASSIA (Quassia).

The stem-wood of *Picrœna excelsa* (Sw.) Lindl.

USES.

A bitter tonic, without astringency; as it contains no tannin it can be ordered with iron preparations.

DOSE.

2 to 8 gr. (0·12 to 0·5 gm.).

PREPARATIONS.

Infusum Quassiæ Concentratum, B.P. (Inf. Quass. Conc.). —Concentrated Infusion of Quassia. Quassia, 1 in 12½, extracted with cold distilled water and preserved with alcohol. This concentrated infusion when diluted with seven times its volume of distilled water yields a preparation which is approximately equivalent in strength, but not in flavour, to fresh infusion of quassia, and differs also in containing a small proportion of alcohol. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

Infusum Quassiæ Recens, B.P. (Inf. Quass. Rec.).—Fresh Infusion of Quassia. 1 in 100. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

NOTE.—If the prescriber wishes the *fresh* infusion to be dispensed, he must specify Inf. Quass. *Recens* on the prescription.

QUILLAIA (Quillaia).

The dried inner part of the bark of *Quillaia Saponaria* Molina, and other species of Quillaia.

USES.

Tincture of Quillaia is used as an emulsifying agent, especially for preparations of tar (e.g. Liquor Picis Carbonis). Expectorant.

PREPARATION.

Tinctura Quillaiæ, B.P. (Tinct. Quill.).—Tincture of Quillaia. 1 in 20, by percolation with alcohol (45%). *Dose*—½ to 1 fl. dr. (2 to 4 mils).

QUINIDINÆ SULPHAS (Quinidine Sulphate).

CHARACTERS.

A white, odourless, crystalline powder, with a bitter taste. *Soluble* 1 in 2200 parts of water.

USES.

Used in auricular fibrillation.

DOSE.

3 to 10 gr. (0·2 to 0·6 gm.).

QUININÆ BISULPHAS (Quinine Bisulphate).

SYNONYM.

Quinine Acid Sulphate.

CHARACTERS.

Colourless, odourless, small needles, very bitter taste, becoming yellow on exposure to light.

Soluble 1 in 10 parts of water, and 1 in 23 parts of alcohol.

USES.

Action similar to quinine sulphate.

DOSE.

1 to 10 gr. (0·06 to 0·6 gm.).

QUININÆ DIHYDROCHLORIDUM (Quinine Dihydrochloride).

SYNONYM.

Quinine Acid Hydrochloride.

CHARACTERS.

A colourless, odourless powder, with a very bitter taste. *Soluble* 1 in 0·6 parts of water, and 1 in 12 parts of alcohol.

USES.
Action similar to quinine sulphate. Used for injection.

DISPENSING.
Solutions for injection may be sterilized by autoclaving, tyndallization or filtration.

DOSE.
By mouth, 1 to 10 gr. (0·06 to 0·6 gm.); by intravenous and intramuscular injection, 5 to 10 gr. (0·3 to 0·6 gm.).

QUININÆ ET ÆTHYLIS CARBONAS (Quinine and Ethyl Carbonate).

CHARACTERS.
Fine, soft, white, matted, needles, odourless, almost tasteless.
Slightly *soluble* in water.

USES.
Action similar to quinine sulphate. Used as a substitute for quinine sulphate, especially for children.

DOSE.
$1\frac{1}{2}$ to 15 gr. (0·1 to 1·0 gm.).

QUININÆ HYDROCHLORIDUM (Quinine Hydrochloride).

CHARACTERS.
Colourless, glistening crystals, very bitter taste.
Soluble 1 in 32 parts of water, and 1 in 2 parts of alcohol (90%).

USES.
Action similar to quinine sulphate.

DISPENSING.
Solutions for injection may be sterilized by autoclaving, tyndallization or filtration.

DOSE.
1 to 10 gr. (0·06 to 0·6 gm.).

QUININÆ SULPHAS (Quinine Sulphate).

CHARACTERS.

Colourless, glistening, crystals, odourless, very bitter taste. *Soluble* 1 in 800 parts of water, and 1 in 65 parts of alcohol.

STORAGE.

Well-closed containers, protected from light. Effloresces rapidly in dry air.

USES.

Tonic, antipyretic, analgesic; malaria curative, and prophylactic.

DOSE.

1 to 10 gr. (0·06 to 0·6 gm.).

PREPARATIONS.

Capsulæ Quininæ Ammoniatæ et Cinnamomi, B.P.C. (Caps. Quinin. Ammon. et Cinnam.).—Capsules of Ammoniated Quinine and Cinnamon. Each capsule contains quinine sulphate, ammonium bicarbonate and oil of cinnamon, and is approximately equivalent to 1 fl. dr. of solution of ammoniated quinine with $\frac{1}{4}$ min. of oil of cinnamon. *Dose*—1 capsule.

Liquor Quininæ Ammoniatus, B.P. (Liq. Quinin. Ammon.).—Ammoniated Solution of Quinine. *Syn.*—Tinctura Quininæ Ammoniata; Ammoniated Tincture of Quinine. It contains 2% w/v of quinine sulphate and 1% w/v of NH_3 in alcohol (60%). 1 fl. dr. contains about 1 gr., and 4 mils contain 0·08 gm., of quinine sulphate. *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

Syrupus Ferri Phosphatis cum Quinina et Strychina B.P. (Syr. Ferr. Phosph. c. Quinin. et Strych.).—Syrup of Ferrous Phosphate with Quinine and Strychnine. *Syn.*—Easton's Syrup. A clear fluorescent syrup, made by dissolving iron wire in concentrated phosphoric acid, and in this dissolving quinine sulphate and strychnine, and filtering into a mixture of glycerin and syrup and adding water. The syrup contains 1 gr. anhydrous ferrous phosphate, $\frac{4}{5}$ gr. quinine sulphate, and $\frac{1}{60}$ gr. strychnine hydrochloride in 1 fl. dr. Tonic. *Dose*—$\frac{1}{2}$ to 1 dr. (2 to 4 mils).

QUININÆ TANNAS (Quinine Tannate).

CHARACTERS.

Pale yellow amorphous powder, with an astringent but only slightly bitter taste.

Slightly *soluble* in cold water; *soluble* 1 in 3 parts of alcohol.

USES.

As for quinine sulphate. Used for children as it is not very bitter in taste.

DOSE.

$1\frac{1}{2}$ to 15 gr. (0·1 to 1·0 gm.).

RESORCINOL (Resorcinol).

SYNONYM.

Resorcin.

CHARACTERS.

White, shining prismatic crystals. On exposure to light it becomes pinkish in colour.

Soluble 4 in 3 parts of water, 1 in 1 part of alcohol (90%), 1 in 1 of ether, and 1 in 20 of olive oil.

STORAGE.

Well-closed containers, protected from light.

USES.

Antiseptic. Used as an ointment for treatment of skin disease, often in combination with zinc oxide.

PREPARATIONS.

Pasta Resorcinolis, B.P.C. (Past. Resorcin.).—Resorcinol Paste. *Syn.*—Pasta Resorcin; Resorcin Paste; Lassar's Stronger Resorcin Paste. Resorcinol, zinc oxide and starch, of each about 20%, with liquid paraffin.

Unguentum Resorcinolis Compositum, B.P.C. (Ung. Resorcin. Co.).—Compound Resorcinol Ointment. *Syn.*—Unguentum Resorcini Compositum; Compound Resorcin Ointment. Resorcinol, 4%, and bismuth subnitrate, 8%, with distilled water, starch, zinc oxide, birch tar oil, and potassium pyrosulphite, in wool fat, ceresin and yellow soft paraffin.

Unguentum Sulphuris et Resorcinolis, B.P.C. (Ung. Sulphur. et Resorcin.).—Sulphur and Resorcinol Ointment. *Syn.*—Unguentum Sulphuris et Resorcini; Sulphur and Resorcin Ointment. Sublimed sulphur, 4·5%, and resorcinol, 3%, in yellow soft paraffin.

RHEUM (Rhubarb).

The rhizome of *Rheum palmatum* Linn. and possibly other species of Rheum.

CONSTITUENTS.

Anthraquinone derivatives and tannoid substances.

USES.

Stomachic, cathartic and astringent.

DOSE.

3 to 15 gr. (0·2 to 1·0 gm.).

PREPARATIONS.

Liquor Rhei Dulcis, B.P.C. (Liq. Rhei Dulc.).—Sweet solution of rhubarb. *Syn.*—Elixir Rhei; Elixir of Rhubarb; Sweet Essence of Rhubarb. Liquid extract of rhubarb, 1 in 4, with oil of anise, syrup, glycerin, alcohol (90%) and distilled water. *Dose*—1 to 3 fl. dr. (4 to 12 mils).

Mistura Rhei et Sodii Bicarbonatis, B.P.C. (Mist. Rhei et Sod. Bicarb.).—Rhubarb and Sodium Bicarbonate Mixture. *Syn.*—Mistura Rhei Composita; Mistura Rhei et Soda. Each fluid ounce contains 4 gr. of rhubarb and 12 gr. of sodium bicarbonate, with oil of peppermint, syrup of ginger and chloroform water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Pilulæ Rhei Composita, B.P. (Pil. Rhei Co.).—Compound Pill of Rhubarb. *Syn.*—Compound Rhubarb Pill. Rhubarb, about 25%, and aloes, about 20%, with myrrh, hard soap, oil of peppermint and syrup of liquid glucose. *Dose*—4 to 8 gr. (0·25 to 0·5 gm.).

Pulvis Rhei Compositus, B.P. (Pulv. Rhei Co.).—Compound Powder of Rhubarb. *Syn.*—Gregory's Powder. Rhubarb, 25%, with heavy magnesium carbonate, light magnesium carbonate and ginger. *Dose*—10 to 60 gr. (0·6 to 4 gm.).

Tinctura Rhei Composita, B.P. (Tinct. Rhei Co.).—Compound Tincture of Rhubarb. Rhubarb, 1 in 10, with cardamom, coriander and glycerin, prepared by percolation with alcohol (60%). *Dose*—½ to 1 fl. dr. (2 to 4 mils).

SACCHARINUM SOLUBILE (Soluble Saccharin).

SYNONYMS.

Glusidum soluble.

CHARACTERS.

A white, crystalline, odourless powder with an intensely sweet taste.

Soluble 1 in $1\frac{1}{2}$ parts of water, and 1 in 50 of alcohol.

USES.

Sweetening agent, and substitute for sugar in diabetes, etc.

DOSE.

$\frac{1}{2}$ to 2 gr. (0·03 to 0·12 gm.).

PREPARATION.

Elixir Saccharini, B.P.C. (Elix. Saccharin.).—Elixir of Saccharin. *Syn.*—Elixir Glusidi; Elixir of Gluside. Saccharin, 1 in 20, with sodium bicarbonate, alcohol (90%) and distilled water. *Dose*—5 to 20 min. (0·3 to 1·2 mil). 1% is sufficient to flavour mixtures.

SALICINUM (Salicin).

CHARACTERS.

Colourless crystals, or white crystalline powder, with a bitter taste.

Soluble 1 in 28 parts of water, and 1 in 80 of alcohol.

USES.

Employed in influenza, and for acute rheumatism.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

SANTONINUM (Santonin).

CHARACTERS.

Minute, colourless, flat rhombic prisms, or white crystalline powder. Becomes yellow on exposure to light.

Almost *insoluble* in water. *Soluble* 1 in 50 of alcohol (90%).

USES.

Anthelmintic, killing the round and thread worms.

DOSE.

1 to 3 gr. (0·06 to 0·2 gm.).

PREPARATION.

Tabellæ Santonini et Scammoniæ Compositæ, B.P.C. (Tab. Santonin et Scammon. Co.).—Compound Tablets of Santonin and Scammony. Each tablet contains $1\frac{1}{2}$ gr. of santonin, 2 gr. of compound powder of scammony and $\frac{1}{2}$ gr. of calomel. *Dose*—1 tablet.

SAPO ANIMALIS (Curd Soap).

CHARACTERS.

The white or greyish-white, horny, and nearly inodorous brittle soap made with sodium hydroxide and a purified solid animal fat. Chiefly sodium stearate.

USES.

Mildly laxative, but chiefly used for its physical qualities.

SAPO DURUS (Hard Soap).

CHARACTERS.

The dry, greyish-white soap, in appearance resembling curd soap, but made with olive oil and sodium hydroxide.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

SAPO MOLLIS (Soft Soap).

CHARACTERS.

A soft unctuous substance varying in colour from yellow to green.

Soluble 1 in 4 parts of water, and 1 in 1 part of alcohol (90%).

PREPARATIONS.

Linimentum Saponis, B.P. (Lin. Sap.).—Liniment of Soap. Soft soap, 8% w/w, and camphor, 4% w/v, with oil of rosemary and distilled water, in alcohol (90%) or industrial methylated spirit suitably diluted.

Liquor Saponis Æthereus, B.P.C. (Liq. Sap. Æther.).—Ethereal Solution of Soap. *Syn.*—Ether Soap; Solutio Saponis Ætherea. A solution containing about 40% of potassium oleate in ether and alcohol (90%), with oil of lavender.

Liquor Saponis Antisepticus, B.P.C. (Liq. Sap. Antisept.)—Antiseptic Solution of Soap. *Syn.*—Antiseptic Ethereal Soap ; Solutio Saponis Antiseptica. Ethereal solution of soap with 0·05% w/v of mercuric iodide, and potassium iodide.

SCAMMONIÆ RESINA (Scammony Resin).

SYNONYM.

Resin of Ipomœa.

CHARACTERS.

A pale brown powder, with an acrid taste. *Soluble* in alcohol (90%), *insoluble* in water, wholly or partly soluble in ether.

USES.

Hydragogue cathartic.

DOSE.

$\frac{1}{2}$ to 3 gr. (0·03 to 0·2 gm.).

PREPARATIONS.

Pilulæ Scammoniæ Compositæ, B.P.C. (Pil. Scammon. Co.).—Compound Scammony Pills. Each pill contains 1 gr. each of scammony resin, jalap resin and curd soap, and $\frac{1}{3}$ gr. of ginger. *Dose*—1 or 2 pills.

Pulvis Scammoniæ Compositus, B.P.C. (Pulv. Scammon. Co.).—Compound Powder of Scammony. Scammony resin, 1 in 2, with jalap and ginger. *Dose*—10 to 20 gr. (0·6 to 1·2 gm.).

SCILLA (Squill).

The bulb of *Urginea Scilla* Steinh., divested of its outer membranes and dried.

STORAGE.

Powdered squill is very hygroscopic, and should be kept in well-closed containers, in a desiccated atmosphere (over lime).

USES.

Expectorant, diuretic, cardiac tonic.

DOSE.

1 to 3 gr. (0·06 to 0·2 gm.).

PREPARATIONS.

Acetum Scillæ, B.P.—A straw-coloured liquid, prepared by macerating bruised squill in dilute acetic acid for 7 days, straining, heating to boiling and filtering. *Dose*—5 to 30 min. (0·6 to 2·0 mils).

Linctus Diamorphinæ et Scillæ, B.P.C. (Linct. Diamorph. et Scill.).—Linctus of Diamorphine and Squill. Each fluid drachm contains $\frac{1}{40}$ gr. of diamorphine hydrochloride and $\frac{1}{20}$ gr. of sodium antimonyltartrate, with liquid extracts of senega and squill, glycerin and syrup. *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

Linctus Scillæ, B.P.C. (Linct. Scill.).—Linctus of Squill. *Syn.*—Linctus; Simple Linctus. Oxymel of squill, 1 in 4, with mucilage of tragacanth, glycerin, emulsion of chloroform and syrup. *Dose*—$\frac{1}{2}$ to 1 fl. dr. (2 to 4 mils).

Oxymel Scillæ, B.P.—A thick, opalescent, brownish liquid, prepared by macerating bruised squill in acetic acid and water for 7 days, pressing, heating to boiling, filtering, cooling and adding purified honey. *Dose*—$\frac{1}{2}$ to 1 dr. (2 to 4 mils) as an expectorant.

Pilulæ Digitalis Compositæ, B.P.C. (Pil. Digit. Co.).—Compound Digitalis Pills. *Syn.*—Pilulæ Digitalis cum Scilla; Guy's Pills; Niemeyer's Pills. Each pill contains 1 gr. each of powdered digitalis, squill, and pill of mercury. *Dose*—1 or 2 pills.

Pilulæ Ipecacuanhæ cum Scilla, B.P.C. (Pil. Ipecac. c. Scill.).—Ipecacuanha Pills with Squill. Each pill contains 2 gr. of powder of ipecacuanha and opium and $\frac{2}{3}$ gr. each of squill and ammoniacum. *Dose*—1 or 2 pills.

Syrupus Scillæ, B.P.—A thick, straw-coloured liquid, prepared by dissolving sucrose in vinegar of squill and water. *Dose*—$\frac{1}{2}$ to 1 dr. (2 to 4 mils).

Tinctura Scillæ, B.P.—A straw-coloured liquid, prepared by macerating bruised squill in alcohol (60%). *Dose*—5 to 30 min. (0·3 to 2 mils).

SENEGA (Senega).

The dried root of *Polygala Senega* Linn.

USES.

A valuable expectorant.

DOSE.

6 to 12 gr. (0·4 to 0·8 gm.).

PREPARATIONS.

Infusum Senegæ Recens, B.P.—Prepared by infusing powdered senega in boiling distilled water for ½ hour. It should be used within 12 hours of its preparation. *Dose*—½ to 1 oz. (15 to 30 mils). Basis for cough mixtures.

Infusum Senegæ Concentratum, B.P.—Concentrated Infusion of Senega. Prepared by percolating senega with alcohol (25%), concentrating, making alkaline by the addition of dilute solution of ammonia and adjusting to volume with more alcohol. When diluted 1 in 8 with water, it gives a preparation approximately similar to Inf. Senegæ Recens.

NOTE.—If the prescriber wishes the *fresh* infusion to be dispensed, he must specify Inf. Seneg. *Recens* on the prescription.

Extractum Senegæ Liquidum, B.P.—Prepared by percolating powdered senega with alcohol (60%) to exhaustion, concentrating, making faintly alkaline with dilute solution of ammonia and adding alcohol (60%) to volume. *Dose*—5 to 15 min. (0·3 to 1 mil).

Tinctura Senegæ.—A brown, sherry-coloured liquid, prepared by diluting the liquid extract of senega 1 in 5 with alcohol (60%). *Dose*—½ to 1 dr. (2 to 4 mils).

SENNÆ FOLIUM (Senna Leaf).

The dried leaflets of *Cassia acutifolia* Delile (Alexandrian Senna) and of *C. angustifolia* Vahl (Tinnivelly Senna).

CONSTITUENTS.

Anthraquinone derivatives.

USES.

Purgative, often given with carminatives on account of its griping action.

DOSE.

10 to 30 gr. (0·6 to 2·0 gm.).

PREPARATIONS.

Confectio Sennæ, B.P.—A soft blackish mass, composed of powdered senna leaf, powdered coriander, figs, tamarind, cassia, prunes, extract of liquorice, sucrose, distilled water; prepared by boiling the figs and prunes in the water, adding the tamarind and cassia, rubbing the pulp through a sieve, in this dissolving the sugar and extract of liquorice and adding the powders, making up to weight with distilled water. Called "Lenitive electuary." *Dose*—60 to 120 gr. (4 to 8 gm.).

Confectio Sennæ et Sulphuris, B.P.C. (Conf. Senn et Sulphur.).—Confection of Senna and Sulphur. Confection of senna and confection of sulphur, equal parts. *Dose*—1 to 2 dr. (4 to 8 gm.).

Tinctura Sennæ Composita, B.P.C. (Tinct. Senn. Co.).—Compound Tincture of Senna. Senna leaf, 1 in 5, caraway and coriander, of each, 1 in 40. *Dose*—For repeated administration, ½ to 1 fl. dr. (2 to 4 mils); for a single administration, 2 to 4 fl. dr. (8 to 16 mils).

SENNÆ FRUCTUS (Senna Fruit).

The dried ripe fruits of *Cassia acutifolia* Delile (Alexandrian Senna) and of *C. angustifolia* Vahl (Tinnivelly Senna).

USES.

Purgative, usually given with carminatives on account of its griping action.

CONSTITUENTS.

Anthraquinone derivatives.

DOSE.

10 to 30 gr. (0·6 to 2·0 gm.).

PREPARATIONS.

Elixir Sennæ, B.P.C. (Elix. Senn.).—Elixir of Senna. *Syn.*—Liquor Sennæ Leguminorum Dulcis; Sweet Essence of Senna Pods. Liquid extract of senna, 1 in 2, with sucrose, chloroform, oil of coriander, tincture of capsicum, alcohol (90%) and distilled water. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

Infusum Senna Concentratum.—Concentrated Infusion of Senna. Prepared by percolating lightly crushed senna fruit 800 with alcohol (20%) and reserving 700 of percolate, continuing until another 1,000 is obtained, concentrating this to a syrupy extract and dissolving it in the first 700, adding strong tincture of ginger 80 and adjusting to 1,000 with more alcohol. When diluted 1 in 8 it gives a preparation approximately equivalent to the fresh infusion.

NOTE.—If the prescriber wishes the *fresh* infusion to be dispensed, he must specify Inf. Sennae *Recens* on the prescription.

Infusum Sennæ Recens.—Fresh Infusion of Senna. Prepared by infusing senna fruit and ginger in boiling distilled water for 15 minutes. *Dose*—½ to 2 fl. ozs. (15 to 60 mils).

Enters into Mist. Sennæ Co. It must be used within 12 hours of its preparation.

Mistura Sennæ Composita, B.P.C.—*Syn.*—Black Draught. An almost black liquid, consisting of magnesium sulphate, liquid extract of liquorice, aromatic spirit of ammonia, compound tincture of cardamom, fresh infusion of senna. *Dose*—1 to 2 fl. ozs. (30 to 60 mils).

Syrupus Ficorum Compositus, B.P.C. (Syr. Fic. Co.).—Compound Syrup of Figs. *Syn.*—Syrupus Ficorum Aromaticus; Aromatic Syrup of Figs. Compound tincture of rhubarb, 1 in 20, liquid extract of senna, 1 in 10, and elixir of cascara sagrada, 1 in 20, in syrup of figs. *Dose*—½ to 2 fl. dr. (2 to 8 mils).

Syrupus Sennæ, B.P. (Syr. Senn.).—Syrup of Senna. Liquid Extract of Senna, 25% v/v, with oil of coriander, sucrose and distilled water. *Dose*—½ to 2 fl. dr. (2 to 8 mils).

SERPENTARIA (Serpentary).

The dried rhizome and roots of *Aristolochia reticulata* Nutt.

USES.

Bitter tonic; employed in dyspepsia.

DOSE.

¾ to 1½ gr. (0·05 to 0·1 gm.).

PREPARATIONS.

Infusum Serpentariæ Concentratum, B.P.C. (Inf. Serpent. Conc.).—Concentrated Infusion of Serpentary. 1 in 2½. When infusion of serpentary or Infusum Serpentariæ is prescribed, this concentrated infusion diluted with seven times its volume of distilled water may be dispensed. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

Tinctura Cinchonæ Composita, B.P. (Tinct. Cinchon. Co.).—Compound Tincture of Cinchone. Extract of cinchone, 5% w/v, dissolved in the liquid obtained by percolating dried bitter-orange peel, serpentary and cochineal with alcohol (70%). It contains 0·5% w/v of the alkaloids of cinchona; 4 mils contains 0·02 gm., and 1 fl. dr. contains about ¼ gr., of alkaloids. *Dose*—½ to 1 fl. dr. (2 to 4 mils).

SEVUM (Suet).

SYNONYMS.

Sevum Præparatum, Prepared Suet.

CHARACTERS.

The white, smooth, internal fat of the abdomen of the sheep (*Ovis aries*) purified by melting and straining.

SODII BENZOAS (Sodium Benzoate).

CHARACTERS.

A white, granular or crystalline powder, with unpleasant sweetish taste.

Soluble 1 in 2 parts of water, and 1 in 50 parts of alcohol (90%).

USES.

Diuretic and urinary antiseptic.

DISPENSING.

Incompatible with acids (precipitate benzoic acid) and with ferric chloride solutions (precipitate ferric benzoate).

DOSE.

5 to 30 gr. (0·3 to 2·0 gm.).

SODII BICARBONAS (Sodium Bicarbonate).

CHARACTERS.

A white powder, or small, opaque, white crystals.

Soluble 1 in 11 parts of water, *insoluble* in alcohol.

USES.

Antacid.

DISPENSING.

Administered as aqueous solution or suspension, as tablets or lozenges. Solutions for injection may be sterilized by filtration, tyndallization or autoclaving. In the latter two methods the solution must be heated in air-tight containers and should not be opened for some time after the solution has fallen to room temperature.

DOSE.

15 to 60 gr. (1 to 4 gm.); 20 gr. make an effervescing draught with $\frac{1}{2}$ oz. lemon-juice. (See Citric Acid.)

20 parts are neutralized by ·16·7 parts of citric acid or 17·8 of tartaric acid.

Enters into Pulv. Efferves. Co., Sodii Phosph. Efferves., Sodii Sulph. Efferves.

PREPARATIONS.

Liquor Alkalinus, B.P.C. (Liq. Alk.).—Alkaline Solution. *Syn.*—Collunarium Alkalinum; Alkaline Nasal Wash. Sodium bicarbonate and borax, of each 1·5% w/v, with phenol and sucrose in distilled water.

Mistura Sodii Carbonatis Aromatica, B.P.C. (Mist. Sod. Bicarb. Aromat.).—Aromatic Sodium Bicarbonate Mixture. *Syn.*—Mistura Carminativa. Carminative Mixture. Each fluid ounce contains 10 gr. of sodium bicarbonate, with aromatic spirit of ammonia, compound tincture of cardamom, glycerin and dill water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Tabellæ Sodii Bicarbonatis Compositæ, B.P.C. (Tab. Sod. Bicarb. Co.).—Compound Tablets of Sodium Bicarbonate. *Syn.*—Soda Mint Tablets. Each tablet contains 5 gr. of sodium bicarbonate, with ammonium bicarbonate, saccharin and ⅛ min. of oil of peppermint. *Dose*—1 to 4 tablets.

Tabellæ Zingiberis Compositæ, B.P.C. (Tab. Zingib. Co.).—Compound Tablets of Ginger. *Syn.*—Ginger Mint Tablets. Each tablet contains 5 gr. of sodium bicarbonate and $\frac{1}{40}$ gr. of oleoresin of ginger, with ammonium bicarbonate, saccharin and ⅛ min. of oil of peppermint. *Dose*—1 or 2 tablets.

SODII BROMIDUM (Sodium Bromide).

CHARACTERS.

A granular, somewhat deliquescent, white powder, or cubic crystals.

Soluble 1 in 1·5 parts of water, and 1 in 16 parts of alcohol.

USES.

Sedative.

DISPENSING.

Incompatible with mercury and silver salts.

DOSE.

5 to 30 gr. (0·3 to 2·0 gm.).

SODII CARBONAS (Sodium Carbonate).

CHARACTERS.

Large transparent, colourless, rhombic crystals.

Soluble 1 in 2 parts of water, *insoluble* in alcohol (90%).

USES.
Alkaline baths and lotions for skin diseases.

DOSE.
5 to 15 gr. (0·3 to 1·0 gm.).

SODII CARBONAS EXSICCATUS (Exsiccated Sodium Carbonate).

CHARACTERS.
A white powder.
Readily *soluble* in water.

STORAGE.
Well-closed containers.

DISPENSING.
3 gr. are equivalent to 8 gr. of the hydrated salt.

DOSE.
2 to 5 gr. (0·12 to 0·3 gm.).

SODII CHLORIDUM (Sodium Chloride).

CHARACTERS.
In small crystalline grains or transparent cubical crystals.
Soluble 1 in 3 parts of glycerin, 1 in 10 parts of glycerin; *insoluble* in alcohol.

PREPARATIONS.
Injectio Sodii Chloridi et Acaciæ, B.P.—A sterile preparation for intravenous injection, prepared by dissolving acacia and sodium chloride in freshly prepared distilled water, autoclaving at 121° to 122° for one hour. When cool, straining through cottonwool and filtering through alternate layers of filter-paper and linen. Transfer to glass containers and again autoclave.

Liquor Dextrosi et Sodii Chloridi, B.P.C. (Liq. Dextros. et Sod. Chlorid.).—Dextrose and Sodium Chloride Solution. *Syn.*—Glucose-saline Solution. A sterile aqueous solution containing 5% w/v of dextrose and 0·9% w/v of sodium chloride.

Liquor Sodii Chloridi Physiologicus.—Physiological Solution of Sodium Chloride. *Syn.*—Normal Saline Solution. A sterile solution of sodium chloride isotonic with blood plasma.

Strength, 0·9% w/v. The sodium chloride 9 is dissolved in *q.s.* distilled water to 1,000, filtered, and sterilized by autoclaving, tyndallization or filtration.

Pulvis Boracis Compositus, B.P.C. (Pulv. Borac. Co.).—Compound Borax Powder. *Syn.*—Pulvis Alkalinus Compositus; Compound Alkaline Powder. Sodium bicarbonate, sodium chloride and borax, equal parts.

SODII CITRAS (Sodium Citrate).

CHARACTERS.

White granular crystals or crystalline powder, with saline taste.

Soluble 1 in 2 of water, *insoluble* in alcohol (90%).

USES.

Antacid. Used to delay clotting of blood (in blood transfusion, etc.); to prevent the formation of curds in milk in the stomach (citrated milk).

DISPENSING.

Solutions for injection may be sterilized by autoclaving, tyndallization or filtration.

DOSE.

¼ to 1 dr. (1 to 4 gm.).

SODII ET POTASSII TARTRAS (Sodium Potassium Tartrate).

SYNONYMS.

Rochelle Salt, Sodii Tartarata.

CHARACTERS.

Colourless crystals or white crystalline powder, with a saline taste.

Soluble 1 in 1·5 parts of water.

Almost *insoluble* in alcohol (90%).

USES.

Diuretic and mild purgative.

DOSE.

2 to 4 dr. (8 to 16 gm.).

PREPARATION.

Pulvis Effervescens Compositus, B.P.—*Syn.*—Seidlitz Powder ; Effervescent Tartarated Soda Powder. Two powders intended to be mixed in cold or warm water and drunk whilst effervescing. No. 1 (wrapped in *blue* paper) containing sodium potassium tartrate 7½, sodium bicarbonate 2½ ; No. 2 (in white paper), tartaric acid 2½.

SODII IODIDUM (Sodium Iodide).

CHARACTERS.

White, granular, crystalline powder, with a saline bitter taste.

Soluble 2 in 1 part of water, 1 in 3 parts of alcohol (90%) and 1 in 1 part of glycerin.

STORAGE.

Well-closed containers.

USES.

As for potassium iodide.

DOSE.

5 to 30 gr. (0·3 to 2·0 gm.).

SODII LACTAS (Sodium lactate, 70%).

CHARACTERS.

Colourless or pale yellow liquid, very viscous.

Soluble in water, alcohol, and glycerin.

USES.

A suggested substitute for glycerin.

SODII METABISULPHIS (Sodium Metabisulphite).

SYNONYMS.

Sodium bisulphite, sodium pyrosulphite.

CHARACTERS.

Colourless crystals. *Soluble* 1 in about 2 of water.

USES.

Antiseptic and antioxidant.

DISPENSING.

Effloresces in air, therefore store in well-closed containers.

SODII MORRHUAS (Sodium Morrhuate).

CHARACTERS.

A yellow or buff-coloured solid.

Soluble in water, but it is of variable composition and a clear solution is not always obtained.

USES.

In 5% solution as a sclerosing solution for varicose veins.

DISPENSING.

Solutions for injection may be sterilized by heating in an autoclave.

PREPARATION.

Injectio Sodii Morrhuatis, B.P.C. (Inj. Sod. Morrh.).—Injection of Sodium Morrhuate. 5% w/v. *Dose*—8 to 75 min. (0·5 to 5 mils), by intravenous injection.

SODII NITRIS (Sodium Nitrite).

CHARACTERS.

Colourless or slightly yellow crystals or granular powder, deliquesces in air.

Soluble 1 in 1·5 parts of water, and 1 in 50 of alcohol.

USES.

Vasodilator. Spiritus Ætheris Nitrosi is used as a diaphoretic.

DISPENSING.

Incompatible with phenazone, acetanilide, caffeine citrate, and oxidizing agents. When Spiritus Ætheris Nitrosi is dispensed with Potassium Iodide, it should be previously neutralized with sodium bicarbonate.

DOSE.

½ to 2 gr. (0·03 to 0·12 gm.).

PREPARATIONS.

Liquor Æthylis Nitritis, B.P.C. (Liq. Æthyl. Nitrit.).—Solution of Ethyl Nitrite. A solution of ethyl nitrite, 2·5 to 3% w/w (equivalent to about 2 to 2·5% w/v) in a mixture of glycerin and dehydrated alcohol. *Dose*—½ to 1 fl. dr. (1 to 4 mils).

Spiritus Ætheris Nitrosi, B.P. (Sp. Æther. Nitros.).—Spirit of Nitrous Ether. *Syn.*—Sweet Spirit of Nitre. An alcoholic solution containing not less than 1·25% and not more than 2·5% w/v of ethyl nitrite, together with acetaldehyde and other related substances. It complies also with a limit test for acid. It should be stored in small, well-closed containers in a cool place and protected from light. *Dose*—¼ to 1 fl. dr. (1 to 4 mils).

Tabellæ Sodii Nitritis Compositæ, B.P.C. (Tab. Sod. Nitrit. Co.).—Compound Tablets of Sodium Nitrite. Each tablet contains ½ gr. of sodium nitrite, ⅓ gr. of diluted erythrityl tetranitrate and 1 gr. of ammonium hippurate. *Dose*—1 or 2 tablets.

SODII PHOSPHAS (Sodium Phosphate).

SYNONYM.

Di-sodium hydrogen Phosphate.

CHARACTERS.

Large, transparent, colourless, rhombic prisms, with saline taste.

Soluble 1 in 7 parts of water.

USES.

Mild diuretic; saline purgative.

DOSE.

½ to 4 dr. (2 to 16 gm.).

PREPARATION.

Sodii Phosphas Effervescens, B.P. (Sod. Phosph. Efferv.).—Effervescent Sodium Phosphate. It contains the equivalent of about 50% of sodium phosphate. It should be stored in well-closed containers. *Dose*—1 to 4 dr. (4 to 16 gm.).

SODII PHOSPHAS ACIDUS (Sodium Acid Phosphate).

SYNONYM.

Sodium Dihydrogen Phosphate.

CHARACTERS.

Colourless, odourless crystals or crystalline powder. *Soluble* 1 in 1 part of water.

USES.

Diuretic, used to render the urine acid; often combined with hexamine in the treatment of infections in the bladder.

DOSE.

30 to 60 gr. (2 to 4 gm.).

SODII SALICYLAS (Sodium Salicylate).

CHARACTERS.

Small colourless crystals, colourless flakes, or white powder. *Soluble* 1 in 1 part of water, and 1 in 6 parts of alcohol.

USES.

Antipyretic, antirheumatic.

DISPENSING.

Incompatible with acids, a precipitate of salicylic acid being formed. Forms coloured solutions with iron salts. If prescribed with quinine salts, the latter should be suspended with Pulv. Trag. Co., and *not* dissolved in acid. Solutions for injection may be sterilized by tyndallization or filtration. Glass containers should comply with the limit tests for alkalinity of glass.

DOSE.

10 to 20 gr. (0·6 to 2·0 gm.).

SODII SULPHAS (Sodium Sulphate).

SYNONYM.

Glauber's Salts.

CHARACTERS.

Colourless crystals, with a bitter saline taste. *Soluble* 1 in 3 parts of water, *insoluble* in alcohol (90%).

USES.

Hydragogue Cathartic.

DOSE.
½ to 4 dr. (2 to 16 gm.).

PREPARATION.
Sodii Sulphas Effervescens, B.P. (Sod. Sulph. Efferv.).—Effervescent Sodium Sulphate. It contains the equivalent of about 50% of sodium sulphate. It should be stored in well-closed containers. *Dose*—1 to 4 dr. (4 to 16 gm.).

SPIRITUS METHYLATUS INDUSTRIALIS (Industrial Methylated Spirit).

A mixture made by a legally authorized methylator, of 19 vols. of alcohol (95%) with 1 vol. of wood naphtha, and is known as 66 O.P. Industrial Methylated Spirits.

STIBOPHENUM (Stibophen).

PROPRIETARY NAME.
Fouadin (*Bayer Products, London*).

CHARACTERS.
Colourless crystalline powder.
Readily *soluble* in cold water, almost *insoluble* in dehydrated alcohol, in ether, in chloroform, acetone and light petroleum.

USES.
In the treatment of schistosomiasis.

DOSE.
1½ to 5 gr. (0·1 to 0·3 gm.), by intravenous injection.

STRAMONIUM (Stramonium).

The dried leaves and flowering tops of *Datura Stramonium* Linn., and of *D. tatula* Linn.

CONSTITUENTS.
0·3 to 0·5% of alkaloid, chiefly hyoscyamine.

USES.
Antispasmodic in asthma.

DOSE.

½ to 3 gr. (0·03 to 0·2 gm.).

PREPARATIONS.

Mistura Lobeliæ et Stramonii Composita, B.P.C. (Mist. Lobel. et Stramon. Co.).—Compound Mixture of Lobelia and Stramonium. Each fl. oz. contains 4 gr. of ammonium carbonate, 5 gr. of potassium iodide and 10 min. each of ethereal tincture of lobelia and tincture of stramonium, in chloroform water. *Dose*—½ to 1 fl. oz. (15 to 30 mils).

Pulvis Stramonii Compositus, B.P.C. (Pulv. Stramon. Co.).—Compound Stramonium Powder. Stramonium, 1 in 2, with lobelia, anise and tea, impregnated with potassium nitrate and oil of eucalyptus.

Tinctura Stramonii, B.P. (Tinct. Stramon.).—Tincture of Stramonium. It is prepared by dilution of liquid with alcohol (45 %), and contains 0·025 % w/v of the alkaloids of stramonium, calculated as hyoscyamine (30 min. contain about $\frac{1}{150}$ gr., and 2 mils contain 0·0005 gm. of alkaloids). It is approximately half the strength of the corresponding preparation of the British Pharmacopœia, 1914. *Dose*—5 to 30 min. (0·3 to 2 mils).

STROPHANTHUS (Strophanthus).

The dried ripe seeds of *Strophanthus Kombé* Oliver.

CONSTITUENTS.

Active principle *K*-strophanthin (a mixture of glycosides).

USES.

Cardiac tonic, similar to Digitalis but more rapid in action.

DISPENSING.

Administered as tincture, or in the form of Strophanthinum, B.P. as intramuscular or intravenous injection.

PREPARATIONS.

Tinctura Strophanthi.—Prepared by defatting powdered strophanthus with light petroleum, drying, repowdering and percolating with alcohol (70 %). The percolate is then assayed biologically and adjusted to the same strength as that of the standard tincture of strophanthus. *Dose*—2 to 5 min. (0·12 to 0·3 mil).

Strophanthinum (Strophanthin).—*Syn.*—Kombé Strophanthin; K. Strophanthin. A mixture of glucosides obtained from strophanthus. It is diluted if necessary with lactose so

as to possess an activity which is 40% of that of anhydrous ouabain. A white or yellowish white powder, moderately soluble in water and in alcohol (90%). It loses its activity in aqueous solution owing to hydrolysis. A solution for injection should be prepared by aseptic methods and transferred to previously sterilized containers. The solution should then be heated to 80° for one hour. It should be used within 24 hours. *Dose*—By intramuscular or intravenous injection, $\frac{1}{240}$ to $\frac{1}{60}$ gr. (0·00025 to 0·001 gm.).

STRYCHNINÆ HYDROCHLORIDUM (Strychnine Hydrochloride).

CHARACTERS.

Small colourless prismatic crystals with a very bitter taste. *Soluble* 1 in 40 parts of water, and 1 in 80 parts of alcohol.

USES.

General tonic.

DISPENSING.

Solutions are incompatible with alkalis, alkali carbonates, iodides, alkaline arsenical solution, and aromatic spirit of ammonia.

Solutions for injection may be sterilized by autoclaving or filtration, and the containers should comply with the limit tests for alkalinity of glass.

DOSE.

$\frac{1}{32}$ to $\frac{1}{8}$ gr. (0·002 to 0·008 gr.).

PREPARATIONS.

Injectio Strychninæ, B.P.C. (Inj. Strych.).—Injection of Strychnine. It contains 0·75% w/v of strychnine hydrochloride; 0·6 mil contains 0·0045 gm., and 5 min. contain about $\frac{1}{30}$ gr. of strychnine hydrochloride. *Dose*—5 to 10 min. (0·3 to 0·6 mil), by subcutaneous injection.

Liquor Strychninæ Hydrochloridi (1% w/v).—A colourless solution of strychnine hydrochloride 1, in alcohol (90%) 25, and distilled water *q.s.* to make 100. *Dose*—3 to 12 min. (0·2 to 0·8 mil). 12 min. contain about $\frac{1}{9}$ gr. of strychnine hydrochloride.

Pilulæ Ferri Phosphatis cum Quinina et Strychnina, B.P.C. (Pil. Ferr. Phosph. c. Quinin. et Strych.).—Iron Phosphate Pills with Quinine and Strychnine. *Syn.*—Pilulæ Trium

Phosphatum; Easton's Pills; Pilulæ Ferri et Quininæ et Strychninæ Phosphatum. Each pill contains $1\frac{1}{8}$ gr. of saccharated iron phosphate, about $\frac{1}{2}$ gr. of quinine sulphate and $\frac{1}{120}$ gr. of strychnine hydrochloride, and is approximately equivalent to $\frac{1}{2}$ fl. dr. of syrup of ferrous phosphate with quinine and strychnine. *Dose*—1 or 2 pills.

Syrupus Ferri Phosphatis cum Quinina et Strychnina, B.P. (Syr. Ferr. Phosph. c. Quinin. et Strych.).—Syrup of Ferrous Phosphate with Quinine and Strychnine. *Syn.*—Easton's Syrup. A clear fluorescent syrup, made by dissolving iron wire in concentrated phosphoric acid, and in this dissolving quinine sulphate and strychnine, and filtering into a mixture of glycerin and syrup and adding water. The syrup contains 1 gr. anhydrous ferrous phosphate, $\frac{4}{5}$ gr. quinine sulphate, and $\frac{1}{80}$ gr. strychnine hydrochloride in 1 fl. dr. Tonic. *Dose*—$\frac{1}{2}$ to 1 dr. (2 to 4 mils).

Tabellæ Ferri Phosphatis cum Quinina et Strychnina, B.P.C. (Tab. Ferr. Phosph. c. Quinin. et Strych.).—Tablets of Ferrous Phosphate with Quinine and Strychnine. *Syn.*—Tabellæ Trium Phosphatum; Easton's Tablets; Tabellæ Eastonii; Tabellæ Ferri et Quininæ et Strychninæ Phosphatum. Each tablet contains about $2\frac{1}{3}$ gr. of saccharated iron phosphate, $\frac{4}{5}$ gr. of quinine sulphate, and about $\frac{1}{80}$ gr. of strychnine hydrochloride, and is approximately equivalent to 1 fl. dr. of syrup of ferrous phosphate, with quinine and strychnine. *Dose*—1 tablet.

STYRAX (Storax).

A semi-transparent, brownish-yellow, semi-fluid balsam obtained from the trunk of *Liquidambar orientalis* Mill.

USES.

Expectorant. Externally as an ointment for skin affections.

DOSE.

10 to 20 gr. (0·6 to 2·0 gm.).

SULPHANILAMIDUM (Sulphanilamide).

SYNONYMS AND PROPRIETARY NAMES.

Prontosil Album (*Bayer Products, London*), Streptocide (*Evans, Sons, Lescher & Webb, Liverpool*), Colsulanyde (*Crookes Laboratories*), P.A.B.S. (*Hewlett & Sons, London*).

CHARACTERS.

Colourless crystals, or crystalline powder.

Soluble 1 in 250 of water at 15·5° C., 1 in 170 at 20° C., and 1 in 115 at 25° C. Sparingly *soluble* in alcohol (95%), *insoluble* in ether, chloroform, and benzene.

USES.

Generally for the treatment of streptococcal infections.

DOSE.

8 to 15 gr. (0·5 to 1·0 gm.).

SULPHAPYRIDINUM (Sulphapyridine).

PROPRIETARY NAME.

Dagenan (*M. & B.* 693) (*Pharmaceutical Specialities* (*May & Baker*) *Ltd.*, *London*).

CHARACTERS.

White crystalline substance.

Soluble 1 in about 3000 of water.

USES.

Treatment of pneumoccoccal infections.

DISPENSING.

Administered orally or in oily suspension, or as a solution of the sodium salt for intramuscular injection.

DOSE.

8 to 60 gr. (0·5 to 4·0 gm.).

SULPHACETAMIDUM (Sulphacetamide).

PROPRIETARY NAME.

Albucid (*Schering*, *London*).

CHARACTERS.

A white powder, *soluble* in water.

USES.

For the treatment of gonorrhœa, and infections of the urinary tract.

DOSE.

7½ to 20 gr. (0·5 to 1·33 gm.).

SULPHATHIAZOLUM (Sulphathiazole).

SYNONYMS AND PROPRIETARY NAMES.

Ciba 3714 (*Ciba, Horsham*), Thiazamide (*M. & B.* 760) (*Pharmaceutical Specialities* (*May & Baker*) *Ltd., London*).

CHARACTERS.

Crystalline white powder.

Slightly *soluble* in water. The sodium salt is *soluble* in water.

USES.

Thought to be of value in staphylococcal, pneumococcal and meningococcal infection.

DOSE.

15 to 60 gr. (1·0 to 4·0 gm.).

SULPHARSPHENAMINA (Sulpharsphenamine).

SYNONYMS AND PROPRIETARY NAMES.

Sulpharsphenobenzene, Sulfarsenol (*Laboratoire Biochemie Médicale, Paris; Modern Pharmacals, London*), Kharsulphan (*Burroughs Wellcome, London*), Metarsenobillon (*May & Baker, London*), Sulphostab (*Boots, Nottingham*), Myosalvarsan (*Bayer Products, London*).

CHARACTERS.

Yellow, odourless powder.

Soluble in water, *insoluble* in alcohol.

STORAGE.

It is packed in sealed glass containers from which the air has been removed, or replaced by an inert gas.

USES.

Antisyphilitic.

DISPENSING.

Solutions for injection may be prepared by dissolving the contents of a sealed container in the requisite amount of sterile, freshly distilled water, and should be used immediately.

DOSE.

By subcutaneous or intramuscular injection, 1½ to 10 gr. (0·1 to 0·6 gm.).

SULPHONAL (Sulphonal).

CHARACTERS.

Colourless, prismatic, tasteless crystals, or white powder. *Soluble* 1 in 450 parts of water.

USES.

Hypnotic.

DOSE.

5 to 20 gr. (0·3 to 1·2 gm.).

SULPHUR PRÆCIPITATUM (Precipitated Sulphur).

SYNONYM.

Milk of Sulphur.

CHARACTERS.

A grey-yellow soft powder, free from grittiness. *Insoluble* in water and alcohol (90%).

USES.

Laxative.

DOSE.

$\frac{1}{4}$ to 1 dr. (1 to 4 gm.).

PREPARATIONS.

Confectio Sennæ et Sulphuris, B.P.C. (Conf. Senn. et Sulphur.).—Confection of Senna and Sulphur. Equal parts of the confections of senna and sulphur. *Dose*—1 to 2 dr. (4 to 8 gm.).

Confectio Sulphuris, B.P. (Conf. Sulphur.).—Confection of Sulphur. Precipitated sulphur, about 40% w/w, and potassium acid tartrate, about 10% w/w, mixed with tragacanth, syrup, tincture of orange and glycerin. *Dose*—1 to 2 dr. (4 to 8 gm.).

Lotio Sulphuris, B.P.C. (Lot. Sulphur.).—Sulphur Lotion. Precipitated sulphur, about 7% w/v, with glycerin, alcohol (90%), rose water and solution of calcium hydroxide.

Trochisci Sulphuris, B.P.C. (Troch. Sulphur).—Sulphur Lozenges. Each lozenge contains 5 gr. of precipitated sulphur.

SULPHUR SUBLIMATUM (Sublimed Sulphur).

SYNONYM.

Flowers of Sulphur.

CHARACTERS.

A fine yellow gritty powder.

Insoluble in water and alcohol (90%).

USES.

Internally as a laxative.

Externally as ointment or lotion as a parasiticide.

DOSE.

$\frac{1}{4}$ to 1 dr. (1 to 4 gm.).

PREPARATIONS.

Unguentum Sulphuris, B.P. (Ung. Sulphur.).—Ointment of Sulphur. *Syn.*—Sulphur Ointment. Sublimed Sulphur, 10%, in simple ointment.

Unguentum Sulphuris Camphoratum, B.P.C. (Ung. Sulphur. Camph.).—Camphorated Sulphur Ointment. Sublimed sulphur and tar, of each 15%, and calcium carbonate, 10%, in lard and soft soap.

SURAMINUM (Suramin).

PROPRIETARY NAME.

Germanin (*Bayer "205"*) (*Bayer Products, London*).

CHARACTERS.

A white or cream powder.

Freely *soluble* in water ; *insoluble* in ether, chloroform, and benzene.

USES.

In the treatment of trypanosomiasis.

DISPENSING

Solutions for injection are prepared by dissolving in sterilized water immediately before use.

DOSE.

15 to 45 gr. (1·0 to 3·0 gm.).

TEREBENUM (Terebene).

CHARACTERS.

An aromatic colourless liquid, consisting of a mixture of dipentene and other hydrocarbons, obtained by agitating oil

of turpentine with sulphuric acid until it no longer rotates a ray of polarized light, and then distilling in a current of steam.

USES.
Expectorant.

DOSE.
5 to 15 min. (0·3 to 1·0 mil).

THEOBROMINA ET SODII SALICYLAS (Theobromine and Sodium Salicylate).

PROPRIETARY NAME.
Diuretin (*Knoll, Ludwigshafen ; Pharmaceutical Products, London*).

CHARACTERS.
A white, odourless, amorphous powder.
Soluble 1 in 1 part of water.

USES.
Diuretic.

DISPENSING.
Incompatible with acids and sodium bicarbonate.

DOSE.
10 to 20 gr. (0·6 to 1·2 gm.).

THEOPHYLLINA ET SODII ACETAS (Theophylline and Sodium Acetate).

PROPRIETARY NAME.
Azurin (*Bayer Products, London*).

CHARACTERS.
A white, crystalline, odourless powder, with a bitter taste.
Soluble 1 in 25 parts of water.

USES.
Diuretic.

DISPENSING.
Incompatible with acids, and sodium bicarbonate.

DOSE.
2 to 5 gr. (0·12 to 0·3 gm.).

THYMOL (Thymol).

CHARACTERS.

Large, colourless, transparent crystals, with aromatic odour and taste.

Soluble 1 in about 1,000 parts of water, and 1 in 1 part of alcohol (90%).

USES.

Antiseptic, Anthelmintic.

DOSE.

½ to 2 gr. (0·03 to 0·12 gm.); as an anthelmintic, 15 to 30 gr. (1 to 2 gm.).

PREPARATIONS.

Glycerinum Thymolis Compositum, B.P.C. (Glycer. Thymol. Co.).—*Compound Glycerin of Thymol. Syn.*—Glycerinum Thymolis Alkalinum. An alkaline solution of thymol with other aromatic antiseptics.

Nebula Mentholis et Thymolis Composita, B.P.C. (Neb. Menthol. et Thymol. Co.).—Compound Menthol and Thymol Spray. Menthol, camphor and phenol, of each 2% w/v, and thymol, 0·2% w/v, in light liquid paraffin.

THYROIDEUM (Thyroid).

SYNONYMS.

Dry Thyroid; Thyroid Extract; Thyroid Gland.

CHARACTERS AND PREPARATION.

A light, dull brown powder, prepared from the fresh and healthy thyroid gland of oxen, sheep, or pigs. The external fat and connective tissue are removed, and the glands cut across. Any which are abnormal are rejected. The healthy glands are minced, dried at a temperature not exceeding 60°, powdered, washed with petroleum spirit to remove all fat, and again dried, assayed and adjusted with lactose to the correct strength.

It is standardized on its iodine content, containing 0·1% of iodine in combination as Thyroxine.

STORAGE.

It should be carefully stored in a well-closed container.

USES.

Increases metabolism. Used in cretinism and myxodœma.

DOSE.

$\frac{1}{2}$ to 5 gr. (0·03 to 0·3 gm.).

PREPARATIONS.

Thyroxinsodium (Thyroxinsodium).—Prepared by the action of sodium carbonate upon thyroxine obtained by the controlled hydrolysis of thyroid gland with barium hydroxide and subsequent purification, or by synthesis. It contains 61% to 65% of iodine.

A white crystalline powder, sparingly soluble in water, unstable with alkalis. *Dose*—$\frac{1}{640}$ to $\frac{1}{64}$ gr. (0·0001 to 0·001 gm.).

NOTE.—When Thyroxine is ordered, Thyroxine-sodium may be dispensed.

TOTAQUINA (Totaquina).

CHARACTERS.

A mixture of the alkaloids from the bark of *Cinchona succirubra* Howard, *C. robusta* Paron and other suitable species of Cinchona. It contains not less than 70% of crystallizable cinchona alkaloids, of which not less than $\frac{1}{5}$ is quinine. A colourless or pale yellowish-grey or pale brown powder, odourless with a bitter taste.

Almost *insoluble* in water.

USES.

Action similar to quinine sulphate.

DOSE.

1 to 10 gr. (0·06 to 0·6 gm.).

TRAGACANTHA (Tragacanth).

CHARACTERS.

A whitish, gummy exudation, in ribbon-like, translucent flakes of horny, curved plates (like the parings of corns), obtained by incising *Astragalus gummifer* Labill and other species of Astragalus. Known as Persian Tragacanth.

USES.

As a suspending agent in the form of Mucilage of Tragacanth or Compound Powder of Tragacanth. It is also often employed as a constituent in hand lotions.

PREPARATIONS.

Lotio Tragacanthæ, B.P.C. (Lot. Trag.).—Tragacanth Lotion. *Syn.*—Lotio Emolliens. Tragacanth, about 0·5% w/v, with spirit of chloroform, tincture of tolu, Cologne spirit, glycerin and distilled water.

Mucilago Tragacanthæ, B.P. (Mucil. Trag.).—Mucilage Tragacanth, 1·25% w/v, with alcohol, in chloroform water. *Dose*—1 to 4 fl. dr. (4 to 16 mils).

Pulvis Tragacanthæ Compositus, B.P. (Pulv. Trag. Co.).—Compound Powder of Tragacanth. Tragacanth, 15%, and acacia, 20%, with starch and sucrose. *Dose*—10 to 60 gr. (0·6 to 4 gm.).

TRINITROPHENOL (Trinitrophenol).

SYNONYM.

Picric Acid.

CHARACTERS.

A bright yellow crystalline powder, with a very bitter taste.

Liable to explode on heat or percussion.

Soluble 1 in 90 parts of water, and 1 in 10 parts of alcohol.

STORAGE.

It is usually stored for safety mixed with an equal quantity of water.

USES.

Antiseptic. Applied as a 1% aqueous solution or as a gauze.

DOSE.

1 to 5 gr. (0·06 to 0·3 gm.).

PREPARATIONS.

Carbasus Trinitrophenolis, B.P.C. (Carbas. Trinitrophen.).—Trinitrophenol Gauze. *Syn.*—Picric Gauze; Picric Acid Gauze. It contains from 1·5 to 2·5% trinitrophenol.

Lotio Trinitrophenolis, B.P.C. (Lot. Trinitrophen.).—Lotion of Trinitrophenol. *Syn.*—Lotio Acidi Picrici; Picric Acid Lotion. Trinitrophenol, 1% w/v, distilled in water.

TRYPARSAMIDUM (Tryparsamide).

CHARACTERS.

A white, odourless, crystalline powder.

Soluble 1 in about 3 parts of water.

USES.

In trypanosomiasis and syphilis.

DISPENSING.

A sterile solution may be obtained by dissolving it in previously sterilized water.

DOSE.

By subcutaneous, intramuscular, or intravenous injection, 15 to 30 gr. (1 to 2 gm.).

UREA (Urea).

SYNONYM.

Carbamide.

CHARACTERS.

Colourless, prismatic, crystals, almost odourless with a cooling saline taste.

Soluble 1 in 1 part of water, and 1 in 1 part of alcohol (90%).

USES.

Diuretic. Used as a test for renal efficiency.

DOSE.

15 to 240 gr. (1 to 16 gm.).

URETHANUM (Urethane).

SYNONYM.

Ethyl carbamate.

CHARACTERS.

Colourless crystals, *soluble* 1 in 2 of water, 1 in 1 of alcohol (95%).

USES.

Hypnotic, diuretic.

With quinine it is used in the treatment of varicose veins.

DOSE.

15 to 30 gr. (1·0 to 2·0 gm.).

VALERIANA (Valerian).

The rhizome and roots of *Valeriana officinalis* Linn collected in the autumn and slowly dried, during which process the characteristic odour develops.

USES.

Antispasmodic.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

PREPARATIONS.

Elixir Valerianæ Compositum, B.P.C. (Elix. Valerian. Co.).—Compound Elixir of Valerian. *Syn.*—Elixir Bromidi et Valerianæ Compositum; Compound Elixir of Bromide and Valerian. 1 fl. oz. contains 7½ gr. each of potassium bromide and chloral hydrate, and 15 m. of liquid extract of valerian, with oils of orange, lemon, coriander and anise, alcohol (95%), syrup and distilled water. *Dose*—15 to 30 mils (½ to 1 fl. oz.).

Mistura Valerianæ Composita, B.P.C. (Mist. Valerian. Co.).—Compound Valerian Mixture. Each fluid ounce contains 10 gr. of potassium bromide and 10 min. of ammoniated tincture of valerian in camphor water. *Dose*—15 to 30 mils (½ to 1 fl. oz.).

Tinctura Valerianæ Ammoniata, B.P. (Tinct. Valerian. Ammon.).—Ammoniated Tincture of Valerian. 1 in 5, by maceration in a mixture of oils of nutmeg and lemon, dilute solution of ammonia and alcohol (60%). *Dose*—½ to 1 fl. dr. (4 to 8 mils).

VENTRICULUS DESICCATUS (Desiccated Stomach).

SYNONYMS AND PROPRIETARY NAMES.

Erythroid (*Oxo, London*), Eugastrol (*Allen & Hanburys, London*), Extomak (*Benger, Manchester*), Gaster Siccata (*British Drug Houses, London*), Gastrexo (*Evans, Sons, Lescher & Webb, Liverpool*), Pepsac (*Boots, Nottingham*), Ventræmon (*Organon Laboratories, London*), Ventriculin (*Parke Davis, London*).

CHARACTERS.

A granular, rough, powder, with slight odour and taste.

USES.

To replace liver extracts in the treatment of certain anæmias.

DOSE.

¼ to 1 oz. (8 to 30 gm.).

VITAMINA (The Vitamins).

VITAMIN A.

Minimum Daily Requirement—About 30 I.U. per kilogramme body weight.

PREPARATIONS CONTAINING VITAMIN A.

Oleum Morrhuæ (Cod Liver Oil).—1 gm. contains about 600 I.U. of Vitamin A, and 85 I.U. of Vitamin D. *Dose*—30 to 120 mins. (2 to 8 mils.).

Oleum Hippoglossi (Halibut Liver Oil).—1 gm. contains not less than 30,000 units of Vitamin A and about 3,000 units of Vitamin D. *Dose*—1 to 5 mins. (0·06 to 0·3 mil).

Liquor Vitamini A Concentratus (Concentrated Solution of Vitamin A).—A solution in fixed vegetable oils (usually arachis) containing 50,000 units of Vitamin A per gramme. *Dose*—1 to 5 mins. (0·06 to 3·0 mil) (250 to 1500 units).

Liquor Vitamini A et D Concentratus (Concentrated solution of Vitamins A and D).—A solution in a fixed vegetable oil containing about 50,000 units of Vitamin A and 5,000 units of Vitamin D. *Dose*—1 to 5 mil (0·06 to 0·3 mil) (2,500 to 12,500 units Vitamin A and 250 to 1,250 units Vitamin D).

Oleum Vitaminatum (Vitaminized Oil).—A solution of Vitamins A and D in fixed vegetable oil, usually arachis oil, containing 1,000 units of Vitamin A and 100 units of Viramin D. *Dose*—15 to 30 mins. (1·0 to 2·0 mil) (1,000 to 2,000 units of Vitamin A, and 100 to 200 units of Vitamin D).

Emulsio Olei Morrhuæ (Cod Liver Oil Emulsion).——A 50% emulsion of Cod Liver Oil, sweetened with Saccharin flavoured with Purified Oil of Bitter Almonds, and preserved with Chloroform. *Dose*—30 to 60 mins. (2·0 to 4·0 mil) (approximately 1,000 to 2,000 units of Vitamin A and 100 to 200 units of Vitamin D).

Emulsio Olei Vitaminati (Emulsion of Vitaminized Oil).—A 50% emulsion of Vitaminized Oil, prepared as Emulsio Olei

Murrhuæ. *Dose*—30 to 60 mins. (2·0 to 4·0 mil) (1,000 to 2,000 units of Vitamin A and 100 to 200 units of Vitamin D).

Extractum Malti cum Oleo Morrhuæ (Extract of Malt with Cod Liver Oil).—Extract of Malt containing 15% v/v of Cod Liver Oil. *Dose*—60 to 240 mins. (4·0 to 16·0 mil) (approximately 650 to 2,500 units of Vitamin A and 65 to 250 units of Vitamin D).

Extractum Malti cum Oleo Vitaminato (Extract of Malt with Vitaminized Oil).—Extract of Malt with 15% v/v of Vitaminized Oil. *Dose*—60 to 240 mins. (4·0 to 16·0 mil) (approximately 650 to 2,500 units of Vitamin A and 65 to 250 units of Vitamin D).

VITAMIN B.

Vitamin B_1.

SYNONYMS.

Aneurine Chloride Hydrochloride Thiamine Hydrochloride.
Minimum Daily Requirement.—About 0·5 mg. per day.

PREPARATION CONTAINING VITAMIN B_1.

Pulvis Vitamin B_1 (Adsorbate of Vitamin B_1).—An adsorbate on Fuller's earth of Vitamin B_1 containing 100 units per gramme. *Prophylactic Dose*—15 to 30 gr. (1·0 to 2·0 gm.) (100 to 200 units). *Therapeutic Dose*—30 to 90 gr. (2·0 to 6·0 gm.) (200 to 600 units). Much larger doses are often given without toxic effects (see p. 447).

Nicitonic Acid (P.P. factor) (see page 313).

VITAMIN C (Ascorbic Acid).—Minimum Daily Requirements.—Infants, 25 mg.; Adults, 50 mg. (For synonyms and doses see page 309.)

VITAMIN D.—Minimum Daily Requirements.—Infants, about 400 units; Children and Adults, about 400 units. Increase during lactation.

PREPARATIONS.

Calciferol (Vitamin D_2).—See page 342.

Preparations of Vitamin D are listed under Vitamin A (page 483–484).

ZINCI OXIDUM (Zinc Oxide).

CHARACTERS.

A soft, white, insoluble, tasteless, impalpable powder.

USES.

Astringent.

DISPENSING.

Applied externally as an astringent to the skin as ointment, paste, or dusting powder.

DOSE.

5 to 10 gr. (0·3 to 0·6 gm.).

PREPARATIONS.

Cremor Zinci, B.P.C. (Crem. Zinc.).—Zinc Cream. Zinc oxide, about 1 in 3, with wool fat, almond oil and solution of calcium hydroxide.

Gelatinum Zinci, B.P. (Gelat. Zinc.).—Gelatin of Zinc. *Syn.*—Unna's Paste. Zinc oxide, 15%, with gelatin, glycerin and water.

Gelatinum Zinci et Ichthammolis, B.P.C. (Gelat. Zinc. et Ichtham.).—Gelatin of Zinc and Ichthammol. *Syn.*—Pasta Zinci et Ichthammolis; Unna's Paste, with Ichthammol. Ichthammol, about 2%, with zinc oxide, glycerin, gelatin and distilled water.

Linimentum Calaminæ Compositum, B.P.C. (Lin. Calamin. Co.).—Compound Liniment of Calamine. Calamine, 1 in 10, with zinc oxide, zinc oleostearate, wool fat, white soft paraffin and liquid paraffin.

Pasta Zinci Oxidi Composita, B.P. (Past. Zinc. Oxid. Co.).—Compound Paste of Zinc Oxide. *Syn.*—Zinc paste, zinc oxide, 25%, with starch and white soft paraffin.

Pulvis Zinci et Amyli, B.P.C. (Pulv. Zinc. et Amyli).—Zinc and Starch Powder. Equal parts of zinc oxide and starch.

Suppositorium Hamamelini et Zinci Oxidi, B.P.C. (Supp. Hamamel. et Zinc. Oxid.).—Hamamelin and Zinc Oxide Suppository. Each suppository weighs 30 gr. (2 gm.) and contains 3 gr. of dry extract of hamamelis and 10 gr. of zinc oxide.

Unguentum Zinci cum Balsamo Peruviano, B.P.C. (Ung. Zinc. c. Bals. Peruv.).—Zinc ointment with Balsam of Peru. Balsam of Peru, about 11%, in ointment of zinc oxide and ointment of boric acid.

Unguentum Zinci Oxidi, B.P. (Ung. Zinc. Oxid.).—Ointment of Zinc Oxide. *Syn.*—Unguentum Zinci; Zinc Ointment. Zinc oxide, 15%, in simple ointment.

ZINCI STEARAS (Zinc Stearate).

CHARACTERS.

A fine, white, amorphous, impalpable powder.
Insoluble in water.

USES.

A mild antiseptic and soothing powder.

ZINCI SULPHAS (Zinc Sulphate).

CHARACTERS.

Small colourless crystals or crystalline powder.
Soluble 1 in 0·7 parts of water, and insoluble in alcohol.

USES.

External astringent.
Internally as an emetic.

DOSE.

1 to 3 gr. (0·06 to 0·02 gm.). As an emetic, 10 to 30 gr. (0·6 to 2 gm.).

ZINGIBER (Ginger).

CHARACTERS.

The dried and scraped rhizome of *Zingiber officinale* Roscoe.

USES.

Carminative, with agreeable aromatic odour and pungent taste.

DOSE.

5 to 15 gr. (0·3 to 1·0 gm.).

PREPARATIONS.

Syrupus Zingiberis, B.P. (Syr. Zingib.).—Syrup of Ginger. Strong tincture of ginger, 5% v/v, in syrup. *Dose*—½ to 2 fl. dr. (2 to 8 mils).

Tinctura Zingiberis Fortis, B.P. (Tinct. Zingib, Fort.).—Strong Tincture of Ginger. *Syn.*—Essence of Ginger. 1 in 2, by percolation with alcohol (90%). *Dose*—5 to 10 min. (0·3 to 0·6 mils).

Tinctura Zingiberis Mitis, B.P. (Tinct. Zingib. Mit.).—Weak Tincture of Ginger. Strong tincture of ginger, 20% v/v, in alcohol (90%). *Dose*—½ to 1 fl. dr. (2 to 4 mils).

INDEX OF POISONS AND THEIR ANTIDOTES

POISONING.—After the accidental swallowing of any strong poison, life sometimes may be saved by causing the patient immediately to swallow a great draught of milk or water to dilute the poison and delay its absorption whilst steps are being taken for the evacuation of the stomach contents. This may be accomplished by emetics or by the stomach-pump, or by tickling the fauces when these agents are not at hand. In poisoning by the strong mineral acids and all escharotic substances the stomach-pump is contra-indicated, but in the case of corrosive substances like carbolic acid this may be used cautiously if a soft tube be employed. Indeed, the soft india-rubber tube of the stomach-pump can scarcely do any harm except in the most destructive instances of poisoning by concentrated sulphuric or nitric acid, and the pump should always be fitted with such a tube in at least two sizes. When at hand the pump should be preferred to every other means of emptying the stomach, and except in the limited number of cases just mentioned, it may even be used when there is room for considerable doubt in the diagnosis of poisoning in patients found in insensible or comatose conditions. The coroner's court will justly censure the practitioner who has been in attendance upon a patient picked up in an insensible condition if the evidence afterwards produced proves that a narcotic poison had been swallowed, though when seen by the physician no such evidence had been forthcoming and the symptoms pointed to head injury, uræmia, or apoplexy. The cautious use of the pump with the rubber tube, when scientifically carried out, can in no way injure the patient's chances of recovery should the case ultimately turn out not to be one of poisoning; and as every minute's delay may be serious for the patient, and as there is thus short time for counsel and debate, he should be prepared to act accordingly and make his error upon the safe side.

The first time of using the stomach-pump is sure to be a bungling affair if the operator feels timorous or nervous. The tongue being depressed by the left index finger as the patient is seated in a chair, with the head well steadied by an assistant, and the gag in position, the tube is to be pushed steadily, boldly, and

rapidly through the mouth, pharynx, and œsophagus till the stomach is reached. Though it is more difficult to pass the soft rubber tube, the confidence in its perfect harmlessness will be of great importance to the novice. He should not be deterred by the sound which may be produced by air passing through the tube as its extremity glides past the epiglottis ; this ceases as the rubber is passed home into the stomach. During the pumping, by reversing the action of the levers, a little water may from time to time be sent into the stomach to clear the tube of any solid obstruction, and before withdrawing it finally, tepid water should be injected into the organ, and this should be pumped out again, the operation being continued till the washings return clear. The antidote may be mixed with the water, and in many instances a quantity of this should be left in the stomach.

The Syphon Tube, with funnel attached, such as is used for lavage of the stomach, may take the place of the stomach-pump in most cases.

30 gr. of sulphate of zinc or 10 gr. of sulphate of copper in a tumblerful of tepid water will prove efficient emetics ; and apomorphine, $\frac{1}{10}$ gr. injected hypodermically, acts with great certainty and rapidity when the patient is unable to swallow.

Mustard in dessertspoonful doses, in copious quantities of tepid water, may be used when the above emetics are not at hand. Ipecacuanha and antimony are too slow in their action to be depended upon.

The contents of the stomach when ejected (or when obtained afterwards upon opening the body) should be carefully preserved for further investigation. This is often overlooked in the exciting period of treatment.

The writer has several times successfully pumped and washed out the stomachs of infants and very young children with a soft india-rubber male catheter, attached to the nozzle of an ordinary large glass or metal syringe.

The following formula may be employed as a *general Antidote for any poison of unknown nature* :

Calcined magnesia, powdered wood charcoal, hydrous peroxide of iron, equal parts of each.

Half an ounce of each of these may be given in a tumblerful of water every half-hour till three doses be taken.

A full dose of adrenalin chloride (well diluted), if given immediately after a lethal dose of strychnine, will cause such blanching of the gastric mucous membrane as to prevent for a time the absorption of the poison. This will give valuable time for the use of antidotal remedies. This expedient is of vital importance in poisoning by the cyanides, and it may be advan-

tageously resorted to after the accidental swallowing of all rapidly acting alkaloidal substances. 5 to 10 gr. Pot. Permang. in solution will act by destroying the poison.

Acetanilid or Antifebrin.—The stomach-pump or an emetic of Carbonate of Ammonia should be used, followed by strychnine, $\frac{1}{25}$ gr. hypodermically, and external warmth. Where cyanosis is marked, inhalations of oxygen may be given, and free stimulation with alcohol.

Acid, Carbolic.—See under Carbolic Acid.

Acids, Mineral.—The stomach-pump should *not* be used. Alkalies—lime, soap, chalk, carbonates or bicarbonates of soda or potash, or magnesia—moderately diluted with water, may be freely given. In the absence of these, plaster off a wall (softened by hot water), oils (almond or olive), and small doses of morphine hypodermically should be administered; all food should be given by the rectum. At a later stage, when the danger of perforation has passed off, bland mucilaginous foods, like barley-water, linseed tea, and white of eggs, may be freely given.

Acid, Prussic (or Hydrocyanic).—The stomach, if possible, should be emptied by the stomach-pump or by a rapid emetic ($\frac{1}{2}$ dr. sulphate of zinc); hypodermic injections of atropine ($\frac{1}{60}$ gr.)—2 mins. of the 1 in 100 solution of atropine may be given, and repeated in 30 minutes if necessary. Ammonia, or whisky, inhalation of oxygen, cold and hot affusions alternately, and *artificial respiration*, are the best agents to resort to.

Freshly precipitated oxide of iron, followed by a solution of carbonate of potassium, is to some extent a chemical antidote, but *free stimulation* after the evacuation of the stomach must be relied upon.

Kossa suggested giving about $\frac{1}{2}$ litre of 3 per cent. solution of potassium permanganate by the mouth immediately and this should be tried when available.

Aconite (and Hellebore or Veratrine).—The stomach-pump or emetics should be used; $\frac{1}{10}$ gr. apomorphine hypodermically, or a tablespoonful of mustard in warm water, or $\frac{1}{2}$ to 1 dr. sulphate of zinc should be given as soon as possible. Stimulants—whisky, and ammonia hypodermically, with 20 to 30 mins. of *Tincture of Digitalis* or 2 mins. Liquor Atropinæ should be then administered. Strychnine may be given ($\frac{1}{20}$ gr.) by mouth, rectum, or hypodermically. 5 to 10 gr. Pot. Permang. should be given in solution if the patient be seen immediately after swallowing the alkaloid.

The patient should be kept horizontally on his back with his head lowered, and in a state of absolute rest, and sinapisms applied to the heart and extremities; and dry heat, friction, and artificial respiration kept up unceasingly.

Alcohol.—The stomach-pump should be promptly used, and after evacuation of its contents the stomach should be filled through it with strong coffee, to which a little ammonia should be added; or a hypodermic injection of 10 mins. Apomorphine solution may be given in the absence of the pump; sinapisms, cold affusion, or electricity may be tried, and in *desperate* cases, where the respiratory centre and heart are rapidly failing, boiling water may be used to cause immediate vesication of the skin over the soles of the feet. The hypodermic injection of $\frac{1}{20}$ gr. strychnine is of unquestionable value, and Mindererus Spirit in 2 oz. doses may be given. Warmth to the surface is essential.

Ammonia and Alkalies.—The stomach-pump should *not* be used. Weak acids (acetic preferable) may be given, largely diluted, and followed by draughts of almond or olive oil or of melted butter, and demulcent drinks. Tracheotomy may be required for the œdema of the glottis, and morphine hypodermically for the shock.

Aniline.—The stomach-pump should be used, and free washing out of the organ accomplished, after which artificial respiration and oxygen inhalations, and strychnine injected hypodermically ($\frac{1}{20}$ gr.). 15 oz. blood should be removed, and 30 oz. saline solution injected into the opened vein or blood transfusion done.

Antimony (Tartar Emetic).—Stomach-pump or emetics are not generally required, as vomiting sets in soon. Tannin, strong tea, or gallic acid, or any diluted astringent tincture or infusion containing tannin, may be freely given, followed up by the hypodermic or rectal administration of alcohol, to which small doses of digitalis or strychnine may be added. White of egg, barley-water, or linseed tea may be given freely, and the patient kept in the prone position.

Butter of Antimony.—The treatment of poisoning by this preparation of Antimony should be the same as for mineral acids—viz. magnesia, soapsuds, chalk, potash, or soda, followed by oil.

Antipyrine.—After stomach-pump, free stimulation by alcohol, followed by hypodermics of strychnine ($\frac{1}{20}$ gr.). External warmth and oxygen inhalations where there is much cyanosis.

Arsenic.—The stomach-pump or emetics, or 10 mins. of apomorphine injection, should be employed even when vomiting has already taken place. Freshly-prepared moist peroxide of iron (prepared by adding soda or ammonia to the tincture of iron), or dialysed iron in ounce doses, diluted, or, in the absence of these, magnesia freely, or animal charcoal, olive oil, or lime water, must be freely given; demulcent drinks and stimulants by mouth or rectum are also indicated. Large doses of castor oil are essential to clear out the intestinal tract and to prevent further absorption.

The following method of using the iron antidote is convenient: 3 oz. of the strong Liq. Ferri Perchloridi is poured into a pint measure, which is filled up with water; 1 oz. of calcined magnesia is then mixed with another pint of water; both solutions or mixtures are then to be thoroughly shaken together, and a dose of one tablespoonful should be given every 5 or 10 minutes.

Atropine and Belladonna.—The stomach-pump or emetics, and afterwards the following are to be given: tannin or tea, charcoal, morphine ($\frac{1}{2}$ gr.) by subcutaneous injection, or laudanum by the mouth, or pilocarpine ($\frac{1}{3}$ gr.) subcutaneously, followed by purgatives. If seen immediately, 5 to 10 gr. Pot. Permang. in solution should be given.

The poison being excreted by the kidneys, the bladder should be emptied by the catheter to prevent reabsorption. Eserine in small doses has been advocated as an antagonist, but pilocarpine is better. Free stimulation and artificial respiration may be necessary.

Camphor.—Stomach-pump or emetics, and copious draughts of water, with brisk saline cathartics, and general counter-irritation, or cold and hot douches alternately, afford the best means of dealing with this poison.

Cannabis Indica.—The stomach-pump or emetics, especially apomorphine hypodermically (10 mins. of B.P. injection), are to be given, and the symptoms treated as they present themselves. It will generally be found necessary both to purge and stimulate.

Cantharides.—Stomach-pump or emetics, mucilaginous drinks, or, in their absence, albumin, chalk, a little opium by the mouth, and a morphine suppository by the rectum, should be used.

Carbolic Acid.—The stomach-pump with its soft rubber tube should be used, after which the organ should be thoroughly washed out with pure glycerin. Alkaline or soluble sulphates, as Epsom or Glauber's Salt, are antidotal, and Schobert gives saccharated solution of lime if the poison is still in the stomach.

Give oils, egg albumin, and warm mucilaginous drinks, with any soluble sulphate, and finally, freely stimulate, counter-irritate, and inject $\frac{1}{60}$ gr. of atropine. Though there is no known antidote, the writer—in a case where half a cupful of the strong acid was taken in a fit of drunkenness—after the contents of the stomach were evacuated, washed that organ out repeatedly with pure glycerin, using half a gallon of it, the glycerin dissolving the excess of acid out of the swollen mucous membrane, and the patient made a good recovery. He has since satisfied himself that this is the best treatment whenever the strong acid has been swallowed; it does not interfere with the administration of soluble sulphates.

Iodine is stated to be a true antidote, and 1 oz. of iodized starch might be advantageously used along with the water employed in washing out the stomach.

Carbon Monoxide (Carbonic Oxide).—Water gas and coal gas owe their poisonous properties to the amount of this agent in their composition. Artificial respiration must be kept up after the removal of the patient from the poisoned atmosphere, and this must be continued for hours. Inhalation of oxygen is to be used at the same time freely, and if the heart shows signs of failure, strychnine may be given, and Faradisation of the phrenic nerves and rhythmic traction of the tongue should be resorted to. If all these fail, and the patient's case appears desperate, venesection should be resorted to, followed by subcutaneous or venous injection of several pints of warm saline solution or a blood transfusion. For CO_2 and acetylene the same measures may be employed.

Chloral Hydrate.—The stomach-pump or emetics, especially 10 min. injections of apomorphine solution, should be used, and these must be followed by injections of strychnine ($\frac{1}{20}$ gr.) or of atropine ($\frac{1}{25}$ gr.), caffeine (5 gr.), or free stimulation with ammonia, whisky, or ether, and sinapisms. *Particularly—external warmth*, electricity, and artificial respiration. The patient should be roused and prevented from sleeping, and, as death may occur from the diminution of the body heat, warmth is essential. A pint of strong, *warm* coffee into the rectum, as advised by Murrell, may save life.

Dougall pointed out that potash is an antidote to chloral, $\frac{1}{2}$ dr. completely decomposing 80 gr. of chloral. He recommends drachm doses of B.P. Liquor Potassæ, largely diluted, every hour.

Chlorine, when inhaled, must be treated by inhalations of ammonia or oxygen, alcohol or Sodii Bicarb. in a respirator, or oxygen subcutaneously. If the poison has been swallowed, it should be neutralized by large quantities of albumin and mucilaginous drinks.

Chloroform.—When symptoms of an alarming interference with the breathing or circulation come on during anæsthesia, the tongue should be drawn forward, artificial respiration, cold affusion, free ventilation by a current of air, turning over the patient upon his left side, or inversion of the body, may be tried.

Hypodermically—whisky, ammonia, strychnine, may be given. Strychnine is unquestionably the best of these, and may be given hypodermically in one dose of 5 to 10 mins. B.P. liquor. Galvanism is doubtful. If the chloroform has been swallowed, use the pump, or give 10 mins. of apomorphine solution, and proceed as if inhaled.

Chronic poisoning or acidosis should be met by intravenous injections of glucose, and calcium salts and large doses of alkalies by the mouth.

Cocaine.—After the stomach-pump or emetics, fill the stomach with hot strong coffee and a little alcohol, and give $\frac{1}{20}$ gr. strychnine. If the symptoms continue, artificial respiration and oxygen inhalation, and if convulsions occur, chloroform, will be necessary.

Coal Gas.—See Carbon Monoxide.

Colchicum.—Stomach-pump or emetics, mucilaginous drinks, albumin, or strong tea or tannin, should be given, and these should be followed by a purgative, after which free stimulation may be required, and symptoms met as they arise.

Conium.—The stomach-pump or emetics, tannin, and castor oil should be used. Stimulate freely by ammonia. Hypodermics of strychnine or atropine may be tried, and artificial respiration persevered with.

Copper Salts.—The stomach-pump or emetics must be resorted to if free vomiting has not occurred ; yellow prussiate of potassium, egg albumin and milk, which form insoluble copper salts, are to be given ; mucilaginous drinks, and wheaten flour or water in which yolks of eggs are suspended, and the free use of opium to allay irritation, are called for.

Corrosive Sublimate.—See Mercury.

Creosote.—The same treatment as for Carbolic Acid.

Croton Oil.—The general treatment for irritant poisons may be used—viz. emetics, or, if in the early stage, the gentle use of the stomach-pump, demulcent drinks, soothing enemata, and opium. Free stimulation and counter-irritation may be necessary.

Cyanide of Potassium.—Poisoning is to be treated as if hydrocyanic acid had been swallowed ; and, if seen at once, give solution of Ferri Sulph. and an alkali ; use the alternate hot and cold douche and give atropine by hypodermic injection. Whilst the poison is in the stomach permanganate of potassium may be given, or its absorption delayed by $\frac{1}{2}$ oz. adrenalin solution.

Digitalis.—The stomach-pump or emetics, especially sulphate of zinc, $\frac{1}{2}$ dr. or 10 mins. of apomorphine solution hypodermically, tannin, or animal charcoal, free stimulation, and the free use of opium are required. Alcohol should be given. The patient should be kept absolutely quiet, and in the horizontal position.

Eserine (or Calabar Bean).—Emetics or the pump, with tannin or any tannin-containing liquid, may be employed, but hypodermic injections of atropine ($\frac{1}{30}$ gr.), till the pupils widely dilate, afford the best chance. Strychnine and chloral have been recommended.

Artificial respiration should be assiduously tried, with friction and warmth externally. If seen immediately after swallowing the poison, 5 to 10 grs. Pot. Permang. in solution should be given.

Ether (Inhalation.)—Pull forward the tongue, give free current of air, commence artificial respiration, and try the Konig-Maas method, and treat as if chloroform poisoning.

Formalin.—Ammonia is decidedly antidotal. Formaldehyde is changed into the comparatively harmless urotropine upon the addition of free ammonia. The best method to pursue in poisoning is to give small doses of ammonia largely diluted with water ; or large quantities of Mindererus Spirit—i.e. the Liquor Ammon. Acetatis every half-hour.

Fungi (or Muscarin).—Emetics or the pump should be used, and atropine given hypodermically ($\frac{1}{40}$ gr.), and repeated till the pupils dilate, or morphine may be given. Free stimulation, sinapisms, and friction may be required.

Gelsemium.—The stomach-pump and emetics are to be used, and bicarbonate of potassium and tannin freely given ; warmth, free stimulation with alcohol, electricity, and artificial respiration.

Hypodermics of ammonia or atropine, or digitalis, are partially antagonistic. Best result will follow 3 mins. of atropine solution.

Hydrocyanic (or Prussic) **Acid.**—Antidote and treatment are described under Acid, Prussic.

Hyoscyamus.—Same as for atropine.

Iodine.—Emetics or the *cautious* use of the rubber tube of the stomach-pump should be employed, together with the free administration of starch, arrowroot, bread, boiled potatoes, or flour, lime water or sodium hyposulphite, and demulcent drinks.

Iodoform.—Emetics or the stomach-pump, and large diluted doses of bicarbonate of soda, followed by free stimulation and a hot pack. Saline solution injected hypodermically in large doses is recommended by Kocher.

Laburnum.—The stomach-pump, if possible, should be always used, even if vomiting has occurred, as portions of seeds, etc., may remain in the stomach. Free stimulation, and, in bad cases, hypodermic injection of ammonia. Counter-irritation, friction, and the cold douche are necessary, after which a brisk purgative should be administered.

Lead Salts.—The stomach-pump, or preferably a large emetic of sulphate of zinc, which is also an antidote, should be given, and followed by milk, white of egg, diluted sulphuric acid, Epsom or Glauber's Salt, or phosphate of sodium, sulphuretted hydrogen, or Harrogate water. Demulcent drinks, with mild opiates to allay pain and spasm, may be administered.

Lime.—Carbonic acid—any aerated water, as soda water or lemonade—is very useful; or weak acetic acid or vinegar, freely diluted, and followed by oil or demulcent drinks, may be swallowed.

Lobelia and Tobacco.—Emetics or the pump should be employed, as should also tannin, and free stimulation externally by sinapisms, friction, and dry heat; internally or hypodermically alcohol, ammonia, and ether, with strychnine ($\frac{1}{20}$ gr.), and small doses of opium. The patient must be kept strictly in the horizontal position.

Luminal.—See Veronal.

Lysol.—See Carbolic Acid.

Mercury (Corrosive Sublimate).—Emetics, or the very cautious use of the soft tube will be required. (The pump should not be used except in the very early stages of the poisoning.) Albumin, or glutin (prepared by washing flour in a muslin bag), demulcent drinks, milk, and oil are to be given by the mouth, and morphine and alcohol subcutaneously.

Methylated Spirits.—See Alcohol.

Morphine.—See Opium.

Muscarin (or Poisonous Mushrooms).—Same treatment as in poisoning by fungi—viz. the subcutaneous administration of atropine after the use of an emetic or the pump.

Nitric Acid.—See under Acids, Mineral.

Nitro-Benzole.—The stomach-pump should be used, and a stream of warm water passed through it. Alcohol and fats must not be used—the main reliance being placed upon counter-irritation by mustard, artificial respiration, and galvanism, and measures useful in prussic acid poisoning.

Nux Vomica.—See Strychnine.

Opium (or Morphine).—The stomach-pump, or, in its absence, emetics (if capable of swallowing), must be resorted to, or $\frac{1}{10}$ gr. of apomorphine injected hypodermically. The stomach should be washed out with tepid water containing potassium permanganate, and filled with strong coffee or tea, or any infusion or liquid containing tannin. Owing to the fact that the mucous membrane of the stomach continues to excrete the poison, it has been advocated that it is of the greatest importance in all severe cases that the stomach be repeatedly washed out at short intervals during the treatment.

Permanganate of potash has been demonstrated to be a chemical antidote to all alkaloids, weight for weight; it can do no harm, and should be given immediately without waiting for vomiting (5 grs. in 2 oz. water). It should be also given after the poison has passed out of the stomach, as it is excreted again by the mucous membrane later on, and the stomach should be repeatedly washed out with the solution. Binet, as the result of much experimentation, has, however, proved that no excretion takes place except in infinitesimal quantity, and he considers that the repeated washings out are valueless. There cannot, however, be any doubt about the great value of washing out the stomach by a solution of the drug at first.

Caffeine, atropine, or strychnine hypodermically is to be administered. This latter should be repeated frequently as long as there are dangerous cardiac or respiratory symptoms; $\frac{1}{50}$ gr. may be given every 2 or 3 hours. Flagellations, cold and hot affusions alternately, electricity, extensive sinapisms, or very hot water, to cause vesication in desperate cases, must be employed to rouse the patient, and when once roused he should never be allowed to fall asleep again, but should be kept continually awake, though every care must be exercised lest this should be carried too far so as to induce exhaustion, as is, unfortunately, often done. Artificial respiration may be required, and this must be kept up assiduously as long as the number of respirations

remains below normal. The dose of atropine should not exceed $2\frac{1}{2}$ mins. of the liquor, and should not be repeated. A larger dose only reinforces the action of the morphia. Venesection followed by saline injection may be necessary.

Oxalic Acid.—The pump or emetics must be used. Lime (lime water, putty of lime, or chalk) is the best antidote; one good dose of castor oil, counter-irritation, free stimulation, and the treatment for gastro-enteric inflammation should be followed.

Phosphorus.—The pump or emetics will be necessary. Sulphate of copper, 5 gr. every 15 minutes, is both antidote and emetic, and the stomach may be freely washed out with a dilute solution of this salt after the contents have been evacuated. Permanganate of potassium, 5 gr. in 1 oz. water, or peroxide of hydrogen, will act as an efficient antidote. French oil of turpentine, or any *old* oil of turpentine, purgatives, and demulcent drinks containing magnesia and albumin should be swallowed. Oils and butter should be avoided.

Physostigma.—See under Eserine.

Pilocarpine.—The stomach-pump or emetics will be required, together with the free administration of tannin and the hypodermic use of its antagonist, atropine, in $\frac{1}{60}$ to $\frac{1}{30}$ gr. doses.

Potash, Caustic.—Emetics must be administered. The pump should *not* be used. Weak acids (vegetable preferred, and largely diluted), oils, and butter may be freely administered. The after-treatment will consist in rectal feeding, and, after the danger of perforation has passed away, the free use of barley-water, linseed tea, and other demulcents.

Potassium Chlorate and Nitrate.—The pump or emetics and profuse demulcent drinks and purgatives are indicated, along with hot blanket baths and the treatment for Acute Bright's Disease.

Ptomaines.—If vomiting has not occurred, the rubber tube should be passed, and the stomach thoroughly washed out with Pot. Permang. Solution or Condy's Fluid. Brisk purgation and lavage of the colon with saline solution should be effected. Heart failure must be met by strychnine hypodermically, or small doses of atropine, and symptoms treated as they arise.

Botulinus toxin can only be combated by injecting the specific serum.

Sewer Gas.—Removal to a pure atmosphere and inhalation of oxygen, with strychnine hypodermically. Warmth to the surface is important, and proceed as in carbon monoxide poisoning.

Silver Nitrate (or Lunar Caustic).—Large doses of common salt or sea water should be swallowed. Emetics and the pump (india-rubber tube) should be used, and white of eggs injected into the stomach after the poison is removed. Yolk of egg, wheaten flour, or milk mixed with water, should be freely administered.

Soda, Caustic.—Acids and Oils will be required (as for Potash).

Stramonium.—Emetics, tannin, free stimulation, and hypodermic use of morphine are the necessary treatment (same as for atropine and belladonna).

Strychnine.—The pump should only be used before spasms have appeared ; emetics, especially a hypodermic injection of $\frac{1}{10}$ gr. apomorphine, must be given, followed by charcoal or tannin in large quantities. Tobacco by rectum (with great caution—not more than 20 gr. at once), bromide of potassium in large doses (2 dr. to 2 oz.), chloral, chloroform, morphine, ether, etc., are recommended. The writer has found by experience that poisonous doses of *Alcohol* afford the best treatment, given both by mouth and rectum. Artificial respiration may be tried. Chloroform inhalation may be kept up as long as the convulsions are severe. If the spasms continue in spite of the above treatment, spinal anæsthesia by the injection of 1 c.c. of Barker's 5 per cent. solution of stovaine may be induced by lumbar puncture. Permanganate of potassium, if given immediately after a poisonous dose, would act as an antidote.

Sulphonal.—Emetics or the use of the stomach-pump ; after the organ has been thoroughly washed out, hot strong coffee should be injected, and a hypodermic dose of strychnine administered. It may be necessary to resort to artificial respiration, which should be assiduously kept up as long as the number of respirations keeps below the normal. A drop of croton oil should be placed on the back of the tongue in cases where the drug has been swallowed a considerable time before the physician has been summoned.

Sulphurets and Sulphuretted Hydrogen.—Inhalation of air containing a small percentage of chlorine in it, and the free administration of a very weak solution of chlorinated lime or soda or iodized starch, constitute the necessary treatment. (See Sewer Gas.)

Sulphuric Acid.—See under Acids, Mineral.

Tartar Emetic.—Tannin, green tea, etc., should be administered. (See Antimony.)

Tobacco.—Emetics, tannin, free stimulation, and hypodermic injection of strychnine ($\frac{1}{20}$ gr.) are indicated, and the recumbent position must be strictly maintained (as for lobelia).

Trional.—Treatment same as for Sulphonal.

Veratrine.—See Aconite.

Veronal.—The stomach-tube should be passed and lavage carried out, strychnine injected hypodermically, and artificial respiration maintained. External warmth must be maintained.

Zinc Salts (chiefly the chloride, as Burnett's Fluid).—The rubber tube of the stomach-pump, if employed, should be used with caution, or emetics, especially apomorphine ($\frac{1}{10}$ gr.), may be injected hypodermically. Egg albumin, oils, tea, tannin, milk, alkalies or their carbonates, and demulcent drinks, should be freely given.

NOTE.—This index has been preserved in Whitla's original form. Directions for "free stimulation" and for the use of alcohol are not in accord with recent evidence. Section I should be consulted.

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